ARCHIVES OF OPHTHALMOLOGY

VOLUME 34 (old series Volume 91) JULY 1945 NUMBER 1

COPYRIGHT, 1945, BY THE AMERICAN MEDICAL ASSOCIATION

ENUCLEATION OF THE EYEBALL

PRACTICAL SUGGESTIONS FOR OBTAINING SATISFACTORY COSMETIC RESULTS

DANIEL B. KIRBY, M.D.

NEW YORK

The operation of enucleation of the eyeball when performed for the relief of intractable pain in cases of absolute glaucoma or severe uveitis may elicit greater expressions of appreciation than surgical procedures which restore vision, as in cases of cataract or detachment of the retina. If, in addition, the cosmetic result in the fitting of a satisfactory prosthesis is excellent, then the happiness of the patient is more than doubled. It is possible to accomplish this. The method I have found most reliable with the least period of disability for the patient is that of simple enucleation or enucleation with immediate implantation of a hollow, nonirritating sphere, such as a gold ball, into Tenon's capsule. The newer alloys may later be found to be satisfactory substitutes for the gold. Glass has been used many times, but there is a desire for a permanent implant. I think there is no contraindication to the use of an implant even in cases of neoplasm or sympathetic ophthalmia, although it may be wise in some of these cases to do a simple enucleation and later, if desirable, to make an implantation of fat into Tenon's capsule. I should not choose to eviscerate the eyeball in cases in which there is no complication. I should, however, consider evisceration the necessary procedure in case of purulent infection of the eye because of the danger of meningitis if the optic nerve and its sheaths are cut across under such conditions.

TECHNIC OF ENUCLEATION IN CASES WITHOUT COMPLICATION

Anesthesia.—Local or general anesthesia may be used. In case of local anesthesia, I have used plenty of procaine hydrochloride, 2 per cent solution, to infiltrate the lids and the anterior and posterior orbital tissues, avoiding the use of more than a minimum of epinephrine hydrochloride. If general anesthesia is employed, attention to the immediate postoperative fluid balance of the patient is important. A 5 per cent solution of dextrose in isotonic solution of sodium chloride may well be given by intravenous or hypodermic injection or rectal clysis to keep the patient from becoming dehydrated.

The operation is then carried out in five steps as follows:

STEP 1: *Incision of Conjunctiva.*—The surgeon may stand at the head of the patient. The eyelids are separated with a solid-bladed speculum. The exposed lashes are trimmed. The pericorneal incision of the conjunctiva is begun at 11

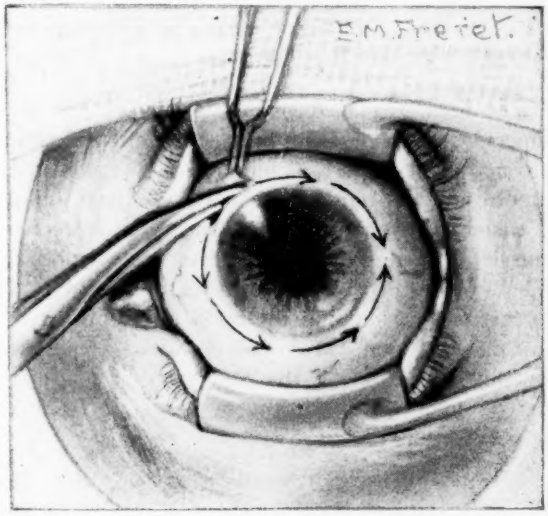

Fig. 1.—Incision of the conjunctiva around the corneal limbus. Note the direction of the incisions.

o'clock on the corneal dial. With undermining and cutting with curved Stevens scissors, the complete circumference is incised in three or, at most, four cuts.

STEP 2: *Section of Rectus Muscle Tendons.*—Tenon's capsule is buttonholed with the same scissors inserted inferotemporally just beneath the external rectus muscle. The muscle hook is slipped carefully and accurately beneath the tendon of the muscle from below up. (It is not swept posteriorly in any uncertain fashion.) The scissors are used to sever the muscle close to its

From the Department of Ophthalmology, New York University College of Medicine and Bellevue Hospital.

This paper was presented at the Forty-Ninth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 11, 1944.

tendinous insertion. In the case of each muscle, the cutting with the scissors is made against the hook so that no delay will be experienced by slipping of the muscle, as may occur if done in the opposite way.[1]

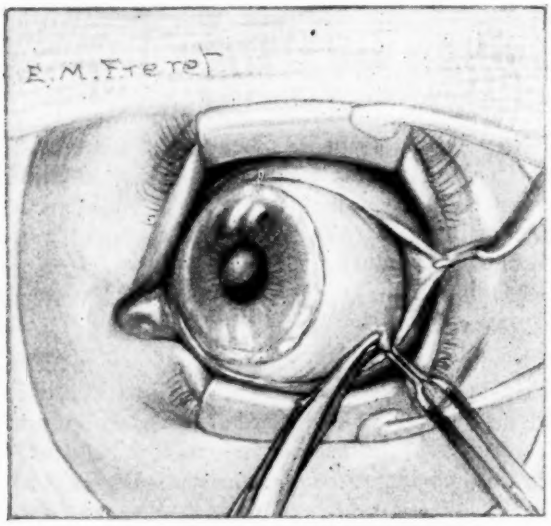

Fig. 2.—Incision through Tenon's capsule beneath the external rectus muscle tendon.

The hook is placed beneath the tendon of the superior rectus muscle from the temporal side (to avoid the superior oblique muscle), and the superior rectus tendon is severed. I have found it easier then to proceed to the inferior rectus muscle, slipping the hook in from the temporal side, cutting the tendon, and then to the internal rectus muscle, slipping the hook up from below. In this dissection, careful observations are made for any extension of the neoplasm or for any staphylomatous protrusion in cases of trauma or perforation.

STEP 3: *Prolapse of Eyeball.*—Now that the four rectus muscles have been severed, the globe may be moderately prolapsed in one of several ways, preferably, in my experience, with two small angulated scleral hooks, one under the stump of the external rectus tendon and the other under the stump of the internal rectus tendon. There is no danger of injury of the nerve posterior to the foramen if due care is exercised. This maneuver has been found to give a most satisfactory position for the next step, that of cutting the optic nerve. The globe may be prolapsed by closing the speculum behind it or by grasping the stump of the interior rectus muscle with fixation forceps. However, the great tendency is for forceps to slip off and not to hold the globe forward.

STEP 4: *Removal of Eyeball.*—Curved enucleation scissors are slipped behind the globe from the nasal side, and the optic nerve, which is placed under moderate tension by prolapse of the globe, is palpated with the blades of the closed scissors. It can easily be felt. The nasal side is chosen because the nerve runs at an angle from the apex of the orbit, which is nasalward, and can easily be straddled just behind the globe. Then the blades of the scissors are slipped backward toward the apex of the orbit, and the nerve is cut at a satisfactory distance behind the globe to avoid intraneural extension of any neoplasm or any deep cupping of the nerve head, as in case of glaucoma or posterior staphyloma. Complete removal of the globe is effected by cutting the attachments of the superior and inferior oblique muscles and of the tissue which is adherent to the globe posteriorly. If the scissors are used on the temporal side, a deeper insertion of the scissors is necessary, and the slanting course of the nerve makes for greater inaccuracy in straddling and cutting the nerve trunk. Care must be exercised not to permit the blades of the scissors to open too far, so that the ends are too far beyond the nerve, to avoid cutting through the muscle–Tenon capsule cone. If such an opening is made posteriorly, it may be possible for the implant to slip through and wander in the orbit.

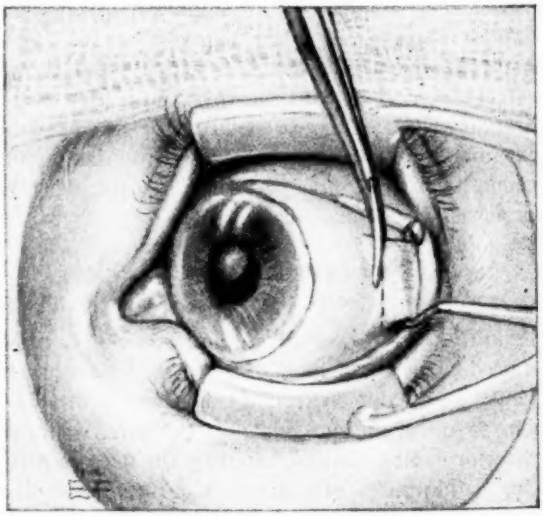

Fig. 3.—Severing of the external rectus muscle tendon with scissors. Note that the incision is made against the hook to prevent the muscle from slipping off.

1. A silk suture for identification is placed most easily in the stump of the external rectus tendon for easier orientation by the pathologist. I have found this preferable to placing the suture in the stump of the superior rectus tendon because of the difficulty of the latter procedure in some cases, particularly with local anesthesia.

I have tried the snare. Even with preliminary severing of the inferior and superior oblique muscles so that they will not be included in the snare, there is much tissue which is close to the posterior portion of the bulb and the nerve that is better

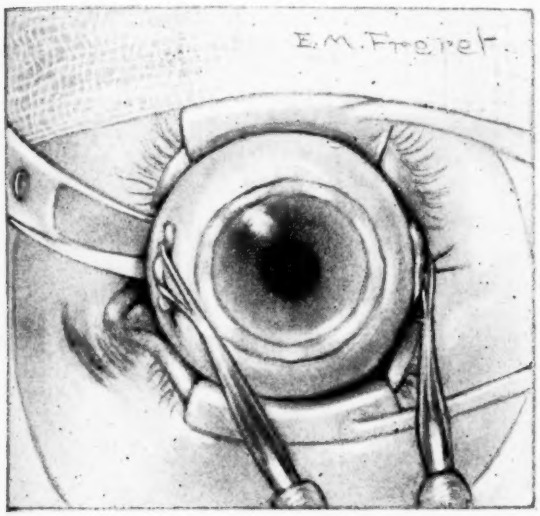

Fig. 4.—Prolapse of the eyeball with bipronged hooks. With enucleation scissors inserted on the nasal side of the globe, the optic nerve is more easily palpated and cut.

cut with scissors after the nerve is sectioned. Hemorrhage after cutting the nerve with scissors can be controlled and has not proved to be a serious factor. If severe hemorrhage is to occur because of the general condition of the patient, the use of the snare will not of itself control it. I have found it best not to apply severe pressure, as with an olive-tipped obturator, and not to use hot gauze packs. In other words, I avoid doing anything which interferes with the vitality and healing of orbital tissue.

STEP 5: *Closure of Incision.*—In simple enucleation the incision may be closed with a simple purse string suture of the conjunctiva, or this may better be freed from the anterior portions of Tenon's capsule and later closed with a buried purse string suture of surgical gut, either plain or 0000, ten day chromic, and then the conjunctiva closed separately with interrupted sutures of plain surgical gut. There may be greater or less undesirable sinking of the orbital tissues after simple enucleation. It is desirable when feasible, to use an implantation into Tenon's capsule.

IMPLANTATION INTO TENON'S CAPSULE

Satisfactory results may be obtained by immediate implantation of a spherical body into Tenon's capsule. Many different shapes and materials, organic and inorganic, have been suggested for this implantation, but the hollow gold ball has stood the test of time. An irregular shape is no better than a smooth sphere. The size should not be over 18 mm. even when an eye enlarged by disease is removed. One which is too large is apt to be worse than none at all.

TECHNIC OF IMPLANTATION PERFORMED IMMEDIATELY AFTER ENUCLEATION

STEP 1: *Dissection of Conjunctiva.*—The globe having been removed as previously described, dissection of the conjunctiva from Tenon's capsule is performed. It should be noted that this dissection was not performed directly after the pericorneal incision of the conjunctiva. This dissection should never be done twice. Less operative trauma is experienced if the dissection is made later. It is easy enough if the assistant with two pairs of forceps holds the conjunctiva, while the surgeon with forceps on Tenon's capsule separates the two with scissors, progressing around the edge of the incision and cutting the tissues back from 6 to 7 mm.

STEP 2: *Insertion of the Sutures.*—Four zero, ten day chromic gut sutures, double-armed with atraumatic needles, are used. Portions of Tenon's capsule found in the four oblique positions, between the four rectus muscles, are selected for the double-overlapping procedure, which has

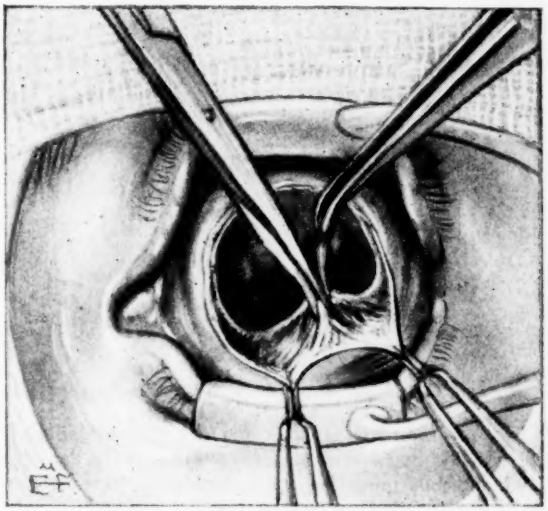

Fig. 5.—Dissection freeing the conjunctiva from Tenon's capsule. This is done for the entire circumference. It is best and most easily accomplished at this stage of the operation.

simply and satisfactorily served to secure the implant in Tenon's capsule–muscle cone without embarrassing the action of the muscles. The two

needles of the double-armed sutures are passed, for example, from inside Tenon's capsule out at 1:30 o'clock, then carried over and passed from within out Tenon's capsule at 7:30 o'clock. Another double-armed suture is passed in similar fashion from 10:30 to 4:30 o'clock.

STEP 3: *Insertion of the Implant.*—This may be done with or without a special instrument. It is simple enough to place the sphere in Tenon's capsule–muscle cone and press it back, while the surgeon or his assistant draws up the strands of the first double-armed suture, forming a single mattress overlap of Tenon's capsule tissue, then quickly follows with the second overlap. Before the second suture is drawn secure, the first suture is tied with a square knot. The suture should be drawn firm and taut but not so tight as to cause pressure necrosis. Then the second suture is tied in similar fashion. Thus there is produced a double overlap of tissue which securely closes Tenon's capsule–muscle cone over the implant. Two muscle hooks are then used to search for openings or exposures of the implant. Usually none are found. If, however, the proper oblique positions are not chosen for the mattress sutures, an area of exposure of the sphere may require another suture, but this is exceptional. The advantage of this suture technic is its simplicity, and the procedure was used with little variation by Wheeler. It does not embarrass the rectus muscles in their action, as may be the effect if the sutures are placed in the muscles vertically and horizontally, drawing them too far forward. The muscles are attached firmly enough to Tenon's capsule so that they do not slip back if they are cut at their tendinous insertions. Care must be exercised not to include the tarso-orbital fascia in the sutures. This structure may be recognized as a white, rather dense tissue. If it is included and brought forward, considerable reduction of motility will result.

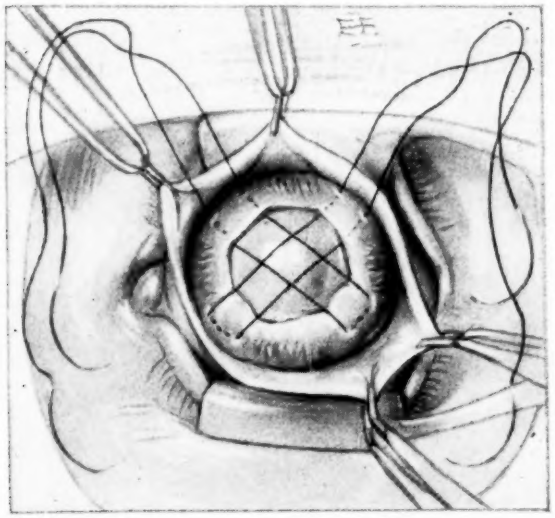

Fig. 6.—Insertion of 0000, ten day chromic surgical gut sutures, double-armed, from within out in diagonal positions, thus preparing for a double mattress overlap of Tenon's capsule over the implant. Note that the four rectus muscles are not included in the sutures. They retract somewhat but retain their function because of their attachments to the investing sheaths of Tenon's capsule.

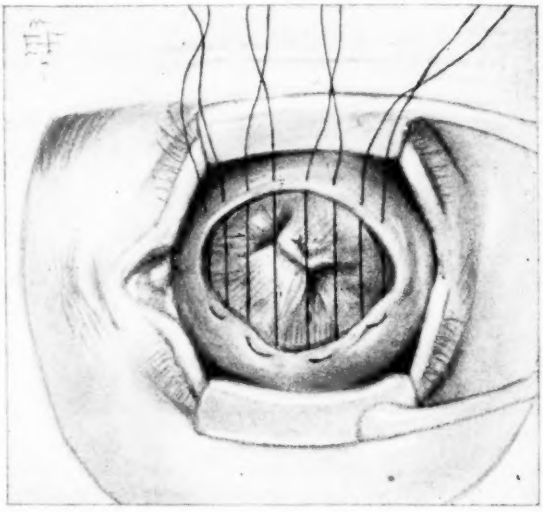

Fig. 7.—The double-overlapping sutures have been tied, effectively burying the implant. The mattress sutures of plain surgical gut are shown ready to close the conjunctiva.

STEP 4: *Closure of the Conjunctiva.*—I have found that a single-armed plain gut suture with atraumatic needle is excellent for closing the conjunctiva. A mattress suture slightly everting the conjunctiva horizontally is used in interrupted fashion. Three or four such sutures usually close the conjunctival incision efficiently. If care is not exercised in accurate appositional closure, granulations may form, which will delay healing. If such do form, they are best cut off with scissors. Caustics should be avoided.

DELAYED IMPLANTATION AFTER SIMPLE ENUCLEATION OR REMOVAL OF AN EYE IN A CASE WITH COMPLICATIONS

In cases in which a definite sinking of the upper lid or upper portion of the orbit develops after healing it is particularly hard to fit a satisfactory prosthesis, for an attempt by the artisan to build up the eye on top in order to fill out the depression does not achieve the desired result at

all but only spreads the lids apart and produces a decided stare. One resort in this situation is to use an implant of fat in Tenon's capsule to fill out the depression. The technic is well described in Wheeler's memorial volume,[2] and it is only necessary to refer the reader to it.

THE DRESSING AFTER ENUCLEATION WITH OR WITHOUT IMPLANTATION

It is important to provide hemostats and to prevent secondary hemorrhage and transudation by proper dressing with moderate pressure. A small amount of nonirritating antiseptic ointment or plain sterile petrolatum is placed over the closed eyelids. Then gauze fluffs are used to fill up to a slight excess the orbital depression within the bony orbital margin. Then 1 inch (2.5 cm.) strips of adhesive tape are applied obliquely from the cheek to the forehead, the skin being drawn up so that the pressure will be held. After this a piece of adhesive tape is placed with sticky side out obliquely across the fellow eye, and a 2 inch (5 cm.) roller bandage is applied firmly, with the turns coming up from below over the side of operation. A pad to protect the ear is excellent. The roller bandage is finally reenforced with adhesive tape. Pressure sufficient to make the dressing efficient in preventing hemorrhage is developed as the bandage is finished.

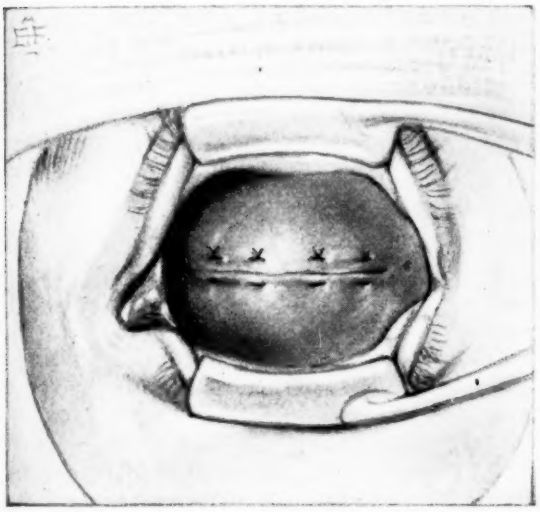

Fig. 8.—Closure of the conjunctiva. The implant is in the muscle cone and is covered with four layers of Tenon's capsule and conjunctiva. The socket when healed is well prepared for the prosthesis.

After-Care.—The dressing is removed after five days, then is refreshed each second day until the patient is ready for a temporary prosthesis. This may well be within ten days to three weeks. If complications develop, they should be taken care of according to indications.

THE PROSTHESIS

The prosthesis is best fitted by an expert artisan. Reform and shell eyes should be such that the artificial eye appears slightly smaller than the fellow eye. If the eye is too large, interference with motility and production of stare are common. The semilunar fold and the caruncle should not be interfered with, as they are essential for any lifelike expression of the eye.

The experienced artisan can help greatly by fashioning an individual prosthesis matching the patient's fellow eye in such respect as the color of the iris, the appearance of the sclera and the distribution of vessels.

Care of the Prosthesis.—Any foreign body in the conjunctiva will cause secretion of mucus, and a glass artificial eye is no exception. The glass from which the prosthesis is made is porous and tends to absorb fluid and material from the conjunctiva. The surface of the prosthesis gradually erodes, roughens and becomes discolored and must be replaced. This process may be delayed somewhat by proper cleaning and polishing, which should be done regularly. The prosthesis should be removed from the socket at night. A satisfactory solution with which to cleanse the prosthesis and the socket is one slightly modified from Lancaster's formula by placing the powder in capsules as follows:

Boric acid	2.00 cc.
Sodium borate	22.00 Gm.
Thymol	0.15 Gm.
Menthol	0.10 Gm.
Oil of eucalyptus	0.40 Gm. (natural oil)
Menthyl salicylate	0.40 Gm. (natural oil)

Pulverize thoroughly. Divide equally into 25 capsules, of 15 grains (0.975 Gm.) each. Keep reserve capsules in a tightly stoppered bottle. This powder must be freshly and individually compounded for this prescription.

Dissolve contents of 1 capsule in ½ pint (one ordinary tumbler) of boiling water. Bottle and use as an eye wash with an eyecup two or three times daily.

Some patients will find a solution of sodium chloride or sodium bicarbonate made with 1 teaspoon of the powder to 1 pint of sterile water more satisfactory.

SUBSTITUTES FOR ENUCLEATION OF THE EYEBALL

Conditions of the eye requiring enucleation usually do not permit of palliative procedures. In the face of absolute glaucoma with no vision remaining and with a sound or partially sighted fellow eye, it is unwise to hazard a procedure which may endanger the fellow eye with the pro-

2. The Collected Papers of Dr. John M. Wheeler, New York, Columbia University Press, 1939.

duction of sympathetic ophthalmia. Filtering operations, cyclodiathermy, cyclectomy and other procedures, such as opticocilioneurotomy, are not without danger in such a situation. If the patient fully understands the situation, he will more readily and gracefully submit to the safer operation.

In conditions of a disfigured, shrunken or moderately contracted but quiet eyeball, which is free from inflammation and has been so for a reasonable time, it may be safe to denude the remains of the cornea of its epithelium and to draw over it a flap of conjunctiva for permanent covering and the fitting of a shell prosthesia. If the eye is staphylomatous, this should not be done because a satisfactory appearance will not be obtained. A large, protruding artificial eye will not give a good cosmetic effect.

CASES WITH COMPLICATIONS

In cases in which extension of neoplasm has developed and is known prior to enucleation or is found at the time of the operation, it may be necessary to revise the plan of enucleation and proceed with evisceration of the contents of the orbit. Immediate grafting of epidermis on the denuded walls and remnants of the contents of the orbit may be done, with prospects of a complete take on bone, periosteum and fat if correct apposition of the graft to the underlying bed is secured by a proper pressure dressing.

If there have been extensive injury of the soft tissues of the orbit and loss of muscle, fat, fascia and production of scar tissue, the socket may need restoration in part or in full after the enucleation.

SUMMARY AND CONCLUSIONS

My experience and technic for performing simple enucleation of the eyeball and enucleation with immediate implantation into Tenon's capsule are given in detail. Relief and safety for the patient and satisfactory cosmetic results have been achieved for patients whose misfortune it is to be forced to submit to removal of the eyeball.

708 Park Avenue.

PRECISIONAL ERRORS IN MEASUREMENT OF SQUINT AND PHORIA

OTTO A. PUTNAM, B.S.
Director of Research, Althouse Chemical Co.
AND
J. VAN DYKE QUEREAU, M.D.
READING, PA.

The purpose of this paper is to examine the degree of precision obtained with the various methods of measuring phoria and squint. It is not its purpose to suggest what degree of precision should be sought; rather, it attempts to show how far present methods may be relied on. Incorrect diagnoses of anomalies of the extraocular muscles can result from lack of attention to certain facts of geometry which profoundly influence such measurements. It is our belief that a higher degree of precision in the measurement of squint and phoria will reveal information not precisely obtainable with present methods.

Three factors comprise the errors in precision in any measurement:

1. Inherent error in means or method.

2. Human error in observation and manipulation.

3. Error in degree of reproducibility, as in high precision determinations of weight or size of an object in which an average of varying results is necessary.

The properties of the human mechanism are seldom constant enough to make the error in reproducibility a serious factor; hence only the inherent and the human errors will be considered.

While it is not always important to measure a single deviation with high precision, it is absolutely essential that good precision attend measurements which will be compared with one another for the purpose of diagnosis of anomalies of the various extraocular muscles. The following data, which may be expressed in any unit, illustrate the manner in which a small error may be magnified when a comparison is made between two measurements:

1. 50 with a + 10 per cent error is actually 45.
2. 40 with a 0 error is actually 40.
3. 51 with a + 2 per cent error in actually 50.
4. 47 with a 0 error is actually 47.

Now, if 1 is compared with 2, the difference is 10, but with an error of 50 per cent. If 3 is compared with 1, the difference is 1, with an error of 500 per cent. If 1 is compared with 4, the difference is 3, but with an error that is wrong even in sign, for 4 is actually 2 units larger than 1, whereas even with 90 per cent precision in measurement of 1 the reverse condition appears to exist. Thus the need for a fairly high degree of precision in measurements for comparison should be apparent.

It is beyond the scope of this paper to illustrate further the theory of significant figures. The point which must generally be remembered in connection with the measurements of phoria and tropia is that a comparison of two measurements differing from each other by an amount equal to, or less than, the precisional error in those measurements is absolutely and completely without meaning and can lead to incorrect and invalid deductions. When the differences are larger than the precisional error by a small amount, the comparison has qualitative but no quantitative significance.

Squint is a manifest directional deviation from the position of a normally functioning eye. Phoria is an overcome tendency toward such a directional deviation. The direction and amount of this deviation from the position of binocular fixation are sought in measuring ocular deviations. Berlin first showed that rotation of the eye is not about a fixed point, but his and subsequent work indicates the variation from a fixed point to be so small that the error introduced by such an assumption is insignificant. All methods herein considered are based on the assumption that rotation of the eye is about a fixed point.

Four past and current means of measuring squint and phoria will be considered: (1) prisms, (2) major amblyoscopes, (3) perimeters and (4) the Hirschberg method. One new means will be analyzed, the (5) Quereau-Putnam Tropophorometer.

PRISMS

INHERENT ERRORS

Error Due to Change in Effectivity of Prisms.—To give a true measurement, a prism would have to be effective, or perform its displacement,

at the center of rotation of the eye. Since this is impossible and the displacement of the visual line must occur outside the eye, the resulting change in effectivity is an inherent error in prism measurement. Since this change in effectivity is caused by the necessity of using the prism away from the center of rotation of the eye, it might possibly be termed a decentering error. It is of real importance in determining large degrees of squint, especially for near point measurements.

The nature of this error is diagrammatically shown in figure 1. It can be seen that the deviation of projection CA from FA is the actual angle of squint. However, ray FP must deviate from FA in order to meet the visual line and

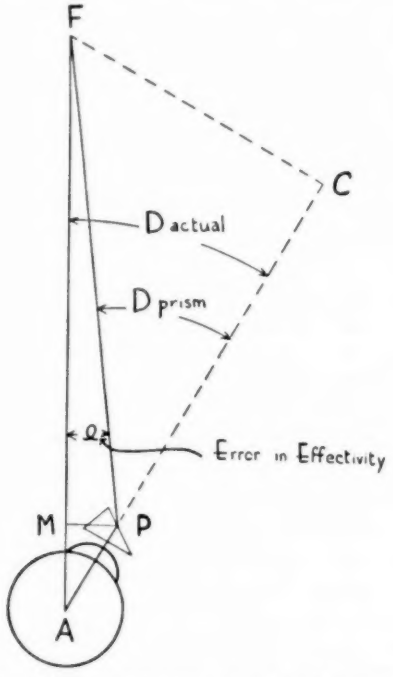

Fig. 1.—Diagram of error due to change in effectivity.

fall on the macula. The prism measures angle FPC, which is larger than the actual angle of squint (FAC) by angle e. This difference between the angle of actual squint and the angle of measured squint is the error due to change in effectivity. It is apparent that movement of the fixation point closer to the eye increases the error, and movement away from the eye reduces the error until at distant fixations FP is substantially parallel to FA, reducing the error to practically zero. It is further apparent that the error would increase as the prism is moved away from the eye along AC and, finally, that the greater the actual angle of squint (FAC) the greater will be the error.

The mathematical considerations follow:

$$Dp = Da - e$$

making

$$e = Dp - Da$$

Since error is the difference between the measured and the actual angle of squint,

$$e = \text{error in effectivity}$$

Consider the magnitude of this error.

$$\sin Dp = \frac{FC}{FP}$$

Hence $$FC = FP \sin Dp \quad (1)$$

Also $$\sin Da = \frac{FC}{AF}$$

Substituting (1) $$\sin Da = \frac{FP \sin Dp}{AF} \quad (2)$$

Also $$\sin Da = \frac{MP}{AP}$$

making $$MP = AP \sin Da \quad (3)$$

Substituting (2) in (3) $$MP = \frac{AP \times FP \sin Dp}{AF} \quad (4)$$

But $$\sin e = \frac{MP}{FP}$$

which, from equation 4, makes

$$\sin e = \frac{AP \times FP \sin Dp}{FP \times AF} = \frac{AP \sin Dp}{AF} \quad (5)$$

While equation 5 expresses the exact size of this error, a fairly close approximation is possible, since in the angles normally measured with prisms the trigonometric sine function is nearly proportional to the angle.

Thus an approximation of equation (5) is:

error = prism-measured angle $\times \frac{AP}{AF}$,

making

$$\% \text{ error} = 100 \frac{\text{distance from center of eye to outer face of prism}}{\text{distance from center of eye to fixated object}}$$

Actual squint = $Dp - Dp \times \%$ error

Thus, the angle measured by a prism is always larger than the actual angle of squint, and the error is a function of the following:

1. Measured angle of deviation
2. Distance of outer surface of prism from center of eye
3. Distance of point of fixation from center of eye.

Suppose an esotropia of 50△ is being measured by the prism and cover test with a fixation light at 13 inches (33 cm.). A 25△ prism is held base out before each eye. Suppose little attention has been given to holding the prisms as close to the eye as possible and that the distance from the center of rotation of the eye to the outer surface of the prism is 2 inches (5 cm.). Applying the formula for the percentage error, the error is found to be 15 per cent, or about 7.7△. The esotropia for near vision, then, is actually only 42.3△. Further, suppose the same 50△ measurement is made with the fixation light at 20 feet (6 meters). Applying the aforementioned formula, the error is found to be a negligible 0.8 per cent. The squint is actually greater for distance than for near vision, the primary cause probably being a divergence in-

sufficiency; but the prism measurement will not show this unless the error in prism effectivity has been accounted for. Had the prisms been held so that their outer faces were the unusually

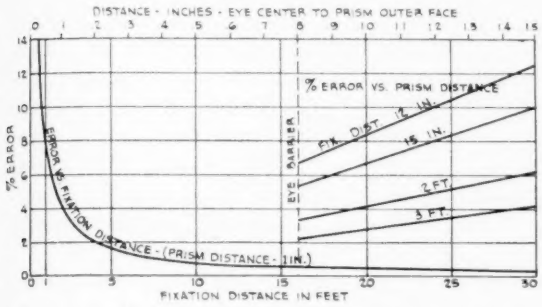
DISTANCE - INCHES - EYE CENTER TO PRISM OUTER FACE
% ERROR VS. PRISM DISTANCE
FIX. DIST. 12 IN.
15 IN.
2 FT.
3 FT.
EYE BARRIER
% ERROR
ERROR VS. FIXATION DISTANCE - (PRISM DISTANCE - 1 IN.)
FIXATION DISTANCE IN FEET

Fig. 2.—Percentage error due to change in prism effectivity.

9.6 per cent. Figure 2 shows the percentage of error plotted against the fixation distance at a prism distance of 1 inch. This is an almost minimum prism distance and is well below the average normally used. The contours of the face are likely to cause increased prism distance from the center of rotation of the eye in measuring in the cardinal directions over that employed in measuring in the eyes front position. The error becomes a large factor in measuring a pronounced vertical deviation combined with a lateral tropia when a thick prism may be held base up or base down over a thick prism held base in or base out. In this case the prism distance is measured along the visual line from the center of rotation of the eye to the outer surface of the outer prism.

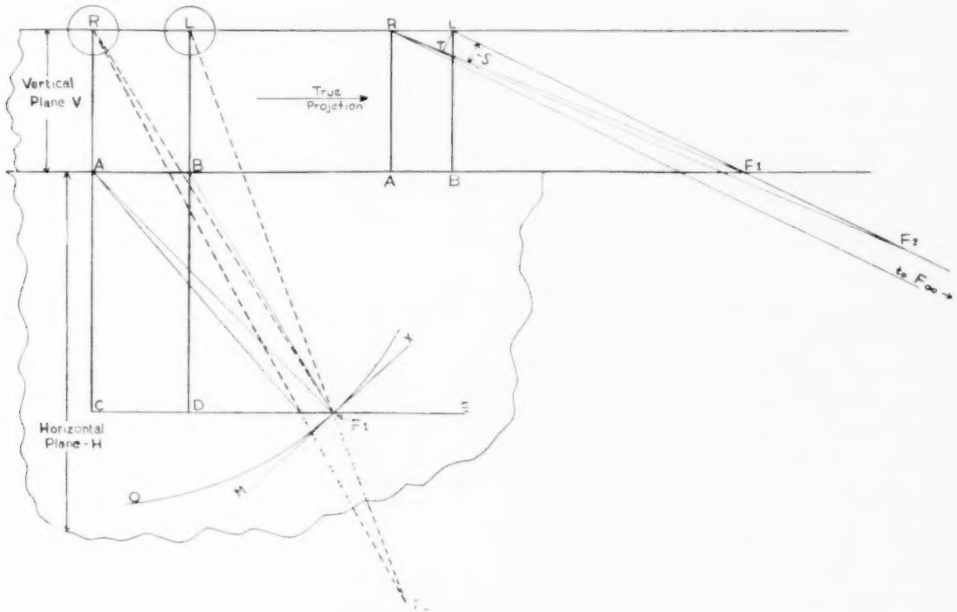

Fig. 3.—Diagram of oblique binocular vision.

small distance of 1 inch (2.54 cm.) from the center of rotation of the eye, the error would have been about 7.5 per cent, or almost 4△. Had the fixation light in the first example been used at 16 inches (40 cm.), rather than 13 inches, the error would have been 6¼△.

Figure 2 indicates the percentage error due to change in prism effectivity, showing the effect both of fixation distance and of distance from the center of rotation of the eye to the outer face of the prism, at which deviation occurs when the prism is held in the Prentice position. At a fixation distance of 13 inches and a prism distance of 1 inch the error is 7.7 per cent, but an increase of the prism distance by only ¼ inch (0.64 cm.) will increase the error to

False Hyperphoria in Oblique Directions.—There is an important geometric factor concerned in measurement of vertical ocular deviations in the four oblique directions. When both eyes look down and to the left, for example, in binocular fixation of a target at a near fixation distance, the visual line of the left eye is depressed a greater number of degrees below the horizontal plane than is the visual line of the right eye. The reason for this is the greater fixation distance of the right eye, due to the lateral separation of the eyes. Since the target distance below the horizontal plane is common to both eyes, the difference in fixation distance necessitates different angles of depression. Near points obliquely viewed in binocular fixation require the eyes to be elevated or depressed at

different degrees above or below the horizontal, the eye nearest the target always being elevated or depressed the greater amount.

This can be illustrated in an exaggerated manner by supposing that the left eye is fixing on an object straight ahead at a distance of 65 mm. from the center of rotation of the eye. Further, suppose that the interpupillary distance is 65 mm. The right eye would be adducted 45°. Now as the fixation point is swung upward about the center of rotation of the left eye, the variation in lateral direction that existed with the eyes looking straight ahead begins to be transferred into vertical deviation, until the left eye would be elevated 90° but the right eye would be elevated only 45° above the horizontal. The geometric considerations as they concern measurement of hyperphoria and hypertropia are diagrammatically shown in figure 3.

Figure 3 is a front isometric diagram of binocular vision downward to the left. The view faces the eyes. Fixation is on F_1, which lies in horizontal plane H. The eyes are in vertical plane V. All lines lying in planes H and V are shown as solid and are in true length. Lines not in these planes are shown as lines of dashes and are not in true length. True projections, in which all lines are shown in true dimension, are shown at the right.

In binocular viewing of F_1, LF_1 is the visual line of the left eye, and RF_1 is the visual line of the right eye. Right triangles RAF_1 and LBF_1 are in vertical planes, including the corresponding visual lines. In the true projections of these triangles, it can be seen that the angles of depression below the horizontal for the two eyes when fixing F_1 are different and the difference is measured by angle S. It is also apparent that the distances from the fixation point to the two eyes differ by RT.

Now if the left eye is the fixing eye and the right eye is covered, the latter may keep the same position, but it is more probable that a small, and normal, diverging movement will occur. Near point exophorias up to 8△ are normal. This normal exophoria results from the fact that focusing functions of an eye are not rigidly related to the convergence mechanism. Thus, the covered right eye assumes a position as though it were fixing a point farther away than the actual target but in the direction established by the fixing eye. The right eye will now have a position as though it were fixing F_2, which lies in a continuation of visual line LF_1. It can be seen in the diagram that in changing from fixation on F_1 to a position equivalent to fixation on F_2, the right eye has moved not only laterally but slightly downward. The vertical movement has in the past been either unknown or not reckoned with.

The vertical component of the diverging movement of the covered eye is shown in the true projection as angle F_1RF_2. This is a source of error in the use of the prism and Maddox rod in measurements of hyperphoria in oblique directions when normal exophoria exists. The prism or Maddox rod is normally held to give horizontal displacement and does not account for this natural vertical component of motion that occurs in the oblique directions. If abnormal lateral phoria is present, serious error is possible.

The visual line of the right eye has shifted along F_1C. The projection of the Maddox rod held so that the line appears straight and level to the patient intersects plane H along line MF_1X. This projection is above the visual line

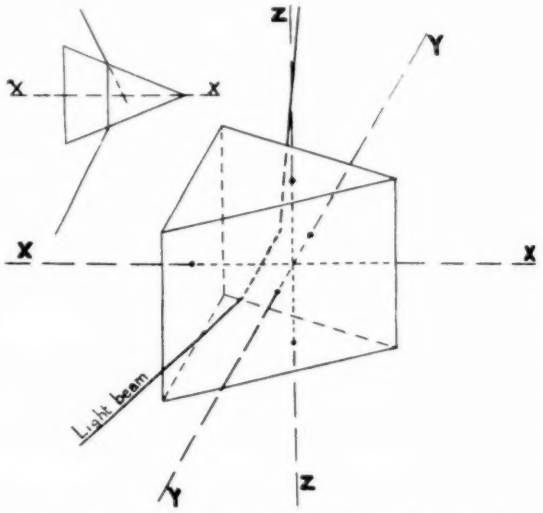

Fig. 4.—Axes for rotation of prism in assuming various positions used in measurement.

RF_2, which makes the Maddox rod appear above the target F_1 as viewed with the fixing eye. An erroneous geometric left hyperphoria is thus indicated as a deviation of the ocular muscles, which in fact does not exist. The Maddox rod is a continuous prism. A single prism displacing the visual line horizontally shifts the projection of the target along the same line as does the Maddox rod, resulting in the same error.

It is interesting to note at this point that if the right eye moved laterally only, and maintained the same angle of depression as in fixing F_1, the visual line would cut plane H along a circle shown as O, the center of which would be at A. The visual line of an eye depressed or elevated at any angle below or above the horizontal will describe a right cone on horizontal movement.

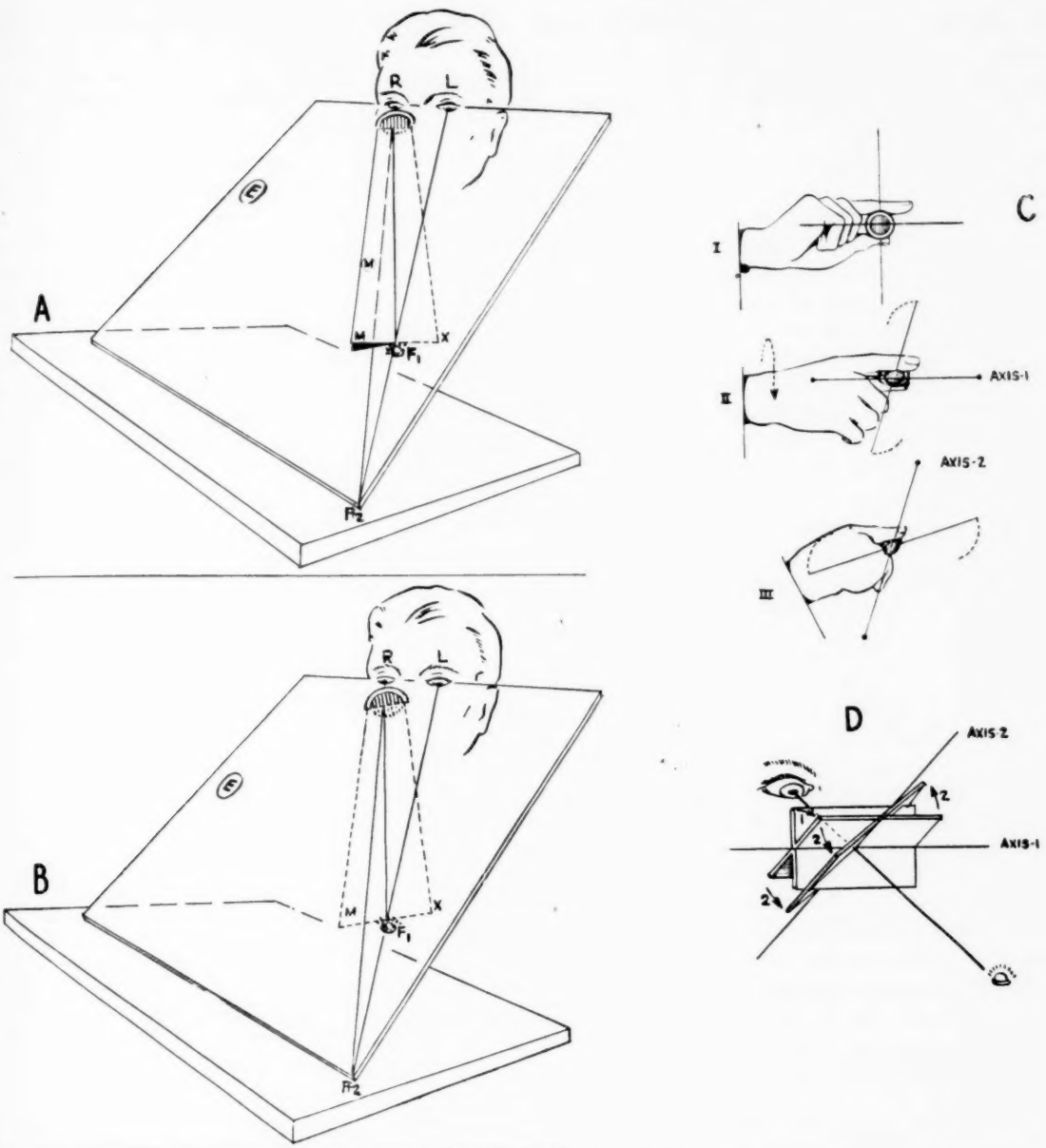

Fig. 5.—False hyperphoria in an oblique direction. *A*, usual manner of holding prisms or the Maddox rod, in which displacement is horizontal, making the Maddox image line appear level. Light from F_1 is changed by the Maddox rod to a plane which is projected outward by the eye as plane *M* and which is seen on edge as a level line. In oblique directions level plane *M* does not coincide with plane *E*, which contains both visual lines LF_1 and RF_1. In cases of exophoria RF_1 moves outward and slightly downward in plane *E* to RF_2. This makes Maddox line MF_1X appear above the light and results in an erroneous diagnosis of left hyperphoria, which actually does not exist. A prism held to give horizontal displacement leads to the same false diagnosis.

B, manner of holding prisms or the Maddox rod to avoid a mistaken diagnosis of left hyperphoria. In this position the projected Maddox plane coincides with plane *E* and does not appear level to the patient. When no pathologic hyperphoria exists, the right visual line RF_1 will now move to RF_2 *along* MF_1X, making the Maddox image line appear to pass through the light in cases of lateral heterophoria.

C and *D*, method of tilting the Maddox rod or prisms to give correct displacement in plane *E*. Two movements are necessary. Movement 1: From vertical position (*I*) rotate the Maddox rod about horizontal axis until it is perpendicular to plane *E*. Movement 2: Rotate the Maddox rod about its now tilted vertical axis until it is perpendicular to a line from the eye to the fixation light. For prisms the surface nearest the eye should be tilted as for the Maddox rod. If the first movement is about the vertical axis, the incorrect position of *A* results.

Actually, prisms can be held to shift the target along line *CE*, thus avoiding the error of a geometric hyperphoria. Rather than being displaced horizontally, the visual line should be displaced or bent in the plane of fixation, as determined by the fixation point and the centers of the two eyes. This is accomplished by keeping the *X* and *Y* axes of a prism, shown in figure 4, in the plane of fixation, as previously indicated. Likewise the Maddox rod held vertical to this plane will give the proper directional displacement to avoid error, although it will not appear level or horizontal to the patient.

Depending on the amount of exophoria present and on how far into the oblique direction the measurement is made, false hyperphoria of varying amounts will be noted, as follows:

False Hyperphoria Present

Direction of Near Fixation	In Exophoria	In Esophoria
Up-left	Right hyperphoria	Left hyperphoria
Up-right	Left hyperphoria	Right hyperphoria
Down-left	Left hyperphoria	Right hyperphoria
Down-right	Right hyperphoria	Left hyperphoria

It will be noted that if esophoria is present the false hyperphorias will be reversed. Obviously, when neither exophoria nor esophoria is present, there is no error. The nature of false hyperphoria can be further illustrated in a simplified manner, as in figure 5. The amount of false hyperphoria that can be measured by use of prism, Maddox rod or nearly opaque red glass can be judged from the following example.

A patient whose pupillary distance is 66 mm. and whose left eye is fixing down at 30° and out at 25° on a point 15 inches (38.1 cm.) distant will show a false left hyperphoria of 2△ when an exophoria of 8△ exists. If an abnormal exophoria of 17△ exists, the false hyperphoria will be 4△. Unless the Maddox rod or prism is held so as to avoid this false hyperphoria when measuring in the cardinal oblique directions, the hyperphoria measured may be greater or less than, or even opposite in direction from, the real pathologic hyperphoria. It is interesting to note that in the example just cited binocular fixation requires the right eye to be depressed 27.7° (as compared with depression of the left eye of 30°) and that the right eye is 16.2 inches (41.2 cm.) distant from the fixing point.

Variable Size of the Prism Diopter.—The true unit of rotational movement is the arc degree; but since employment of prisms is a common method of measuring squint and phoria, the practice of using prism units (the tangent prism diopter) is rather prevalent. The prism diopter is based on a system which makes it a constant unit of displacement; but when it is somewhat invalidly used as a unit of rotational deviation, it becomes a variable unit. This is because a unit of displacement at a larger deviation requires less angular rotation than at smaller deviations. Figure 6 shows the changing value of the prism diopter when used as a unit of rotational deviation. The value is given in terms of the arc degree which is a true unit of rotational deviation.

In the prism range of 30△ (16.7°) the value of the prism diopter decreases from 0.576° to 0.525°, or approximately 10 per cent. Because of this, ten times 1△ is not 10△, nor is 20△ added to 20△ equal to 40△. An angle of 21.8° could be measured with one 40△ prism or with two prisms of 19.3△ each, totaling 38.6△. This results in a 3.5 per cent error. At larger angles the error becomes increasingly greater.

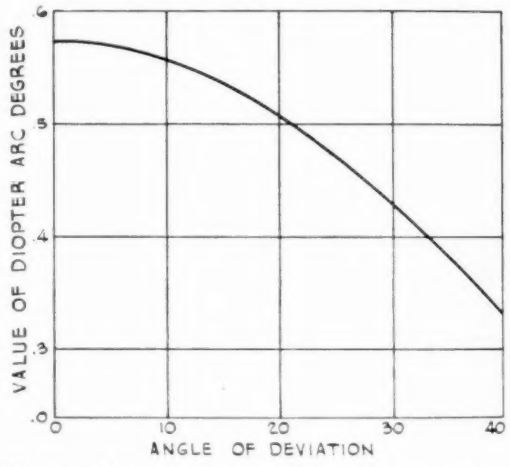

Fig. 6.—Value of the diopter at varying angles of deviation.

Normal usage in measuring large angles is helpful. A squint measured with two 25△ prisms is called a 50△ squint. The angle is actually 28.1°, or 53.3△, but the practice of adding the separate measurements reduces the error resulting from the varying unit. The prism diopter is roughly 0.5 arc degree. Unless this assumption is used in determinations, it is not a source of error. The sole source of error is in the variation of the value of the prism diopter when used as a rotational unit. That such a system of measuring angular deviation of the eye is subject to inherent error is obvious. While errors of the magnitude encountered in this system are not always significant, their presence should be recognized if not actually accounted for. They are of sufficient magnitude to affect

conclusions drawn from measurements for comparison.

HUMAN ERROR OF MANIPULATION

Variable Prism and Target Distances.—The human error of manipulation can greatly affect the inherent error in effectivity. The distance of the prism from the eye can easily vary from one measurement to another. The size of the error and the effect of prism distance were pointed out previously. Likewise, the distance of the fixing object, such as a small light, may easily vary a few inches. In this way, the human error is again injected into the error in effectivity, to a degree previously shown in figure 2. Figure 7 is a diagrammatic illustration.

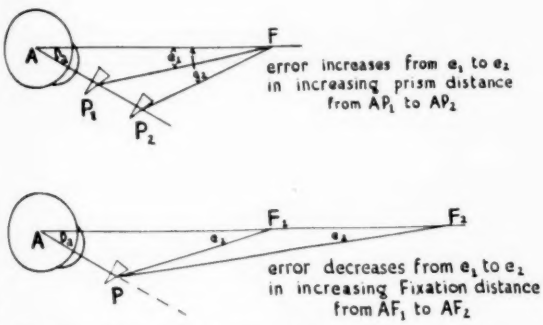

Fig. 7.—Variation of error in effectivity with changing prism and fixation distances.

Another factor in prism measurement is the human error possible in measuring in the cardinal directions. While measurements of squint and phoria in any of the cardinal directions are in the field of action of the various ocular muscles, it is important to know how far into the field the measurement is being made if the results are to bear good quantitative significance. It is not easy to judge the exact angle of a target from the horizontal and vertical planes.

Changes of Prism Strength with Rotation.—Still another human error in manipulation is found in the error due to variation of the prism from its theoretically proper position. Rotation about the Z axis (fig. 4) is the most serious variation affecting precision. A most thorough and searching treatment of this by Dr. Le Grand Hardy[1] is concurrently published with this paper. It completely covers the serious errors encountered in rotation about the Z axis.

Rotation about the Y axis tends to rotate the bending plane and thus to turn horizontal bending into vertical bending. A prism held base in or base out before the eyes can be rotated through 5° without appreciable effect on the lateral measurement. However, the prism is in a position to affect maximally the vertical component of bending. If a lateral correction is made prior to measuring a vertical deviation, their vertical axes pass through the centers of error in the vertical measurement. This can easily be shown by holding a Maddox rod in front of the eye horizontally. A 20△ prism is held base in before the same eye, and, without the Maddox rod being moved, the prism is rotated slightly. Without considerable care in holding compensating prisms, error up to 2△ can easily be injected into the measurement being made at right angles to it.

Rotation about axis X (fig. 4) causes an insignificant error, although there is some effect, as can be demonstrated by viewing a vertical straight line, such as a door frame, through a prism held base in or base out. If the viewer is within 6 feet (182.8 cm.) of the door, the frame will appear bowed, as the result of different angular passages through the prism as he looks from the top to the bottom of the door.

AMBLYOSCOPES

Measurement of tropia and phoria with any of the various modifications of the amblyoscope does not involve any inherent precisional errors. However, in practice, their vertical axes are usually placed well forward of the center of rotation of the eye in order to accommodate esotropia. Unless these axes are placed forward of the center of rotation of the eye, the reflecting mirrors or prisms interfere with one another or with the nose. This forward position of the axes introduces a decentering error, or error in effectivity, exactly in the manner previously explained with prisms. At distance fixations the error is of no consequence, but at near points of fixation this practice is the source of substantial and significant error.

The human error in observing scale readings should not be significant if they can be read to 0.25°, or ½△.

There is a source of human error on the part of the patient in measurement with amblyoscopes. The use of lenses to create an artificial fixation distance does not bring into play the psychic factors affecting the conception of distance. Thus, when the psychic sense of distance is strong, considerable variation in lateral measurements will occur, introducing precisional errors of variable, unpredictable and indeterminate magnitude.

1. Hardy, LeG.: Clinical Use of Ophthalmic Prisms (Metric), Arch. Ophth., this issue, p. 16.

PERIMETERS

Perimeters are primarily designed to measure the field of vision. For this reason they are almost universally made to give readings or data in the polar coordinate system, which is most desirable in perimetry. This limits the direct reading of lateral tropia to the horizontal plane and the direct reading of vertical tropia to the vertical plane directly in front of the measured eye. Aside from direct readings in these limited directions, considerable mathematical computation must be made to determine lateral and vertical tropias. This is necessary to determine vertical or lateral deviations from polar coordinate data.

No inherent errors are encountered if the nonfixing eye is kept in the center of the measuring arc to avoid a decentering error. However, considerable ingenuity is necessary in choosing target positions so that the proper reference position for the nonfixing eye is known. While the perimeter is admirably suited to measurement of the visual field, this instrument is practically useful in the measurement only of lateral tropia in the horizontal position. As the instrument is generally used, the degree of precision obtained is not sufficient to warrant deductions from comparative measurements, for instance, a comparison of measurements for near and distant fixation.

HIRSCHBERG REFLEX METHOD

The Hirschberg method is particularly useful in measuring tropias in very young children when more accurate methods are not practical. It is also useful for patients who do not have central fixation in the squinting eye and whose squint must be measured objectively.

When the squint is to be measured at the near distance, the patient fixes a light held at 33 cm. in front of his fixing eye. The examiner's eye is placed behind the light and in line with it and the patient's squinting eye. The position of the light reflex on the squinting eye is then noted. Each millimeter of displacement of the light reflex from the center of the cornea of the squinting eye equals 7° of arc. An approximate allowance for the angle κ as observed in the fixing eye should be made.

If the position of the reflex can be measured by a millimeter rule, the precision of the measurement is slightly over 0.5 mm. In the case of young children who will not permit a rule to be placed in front of the eyes, the examiner must judge the distance of the reflex from the center. In this case judgment to within 1 mm. is all that can be expected, and hence the precision is not better than 7°. When a rule can be used, the precision is about 5°, or certainly no better than 4°.

The measurement at distance fixation is the weak point in the Hirschberg method. The average convergence at near point fixation is about 10°. In measuring at distance fixations a new reference light position must be used, or this 10° becomes a source of error, causing the measurement of a convergent squint to be 10° less, and that of a divergent squint 10° more, than the actual value. To avoid this, either the distant object must be the source of light for the corneal reflection or a near light must be shifted into a line connecting the squinting eye with the distant object. It is difficult to insure proper fixation for a child at distance with the examiner's head so close to the line of fixation. The precision of the Hirschberg method at distance is not better than 7 or 8° of arc. Therefore, comparisons with near point values for tropia contain a precisional error of 11° to 14°.

THE QUEREAU-PUTNAM TROPOPHOROMETER

The present understanding of the action, functions and motivations of the ocular muscles has advanced to a point which makes errors of the magnitude just mentioned a serious shortcoming in diagnosis. Efforts toward the end of reducing precisional error to a minimum in the measurement of tropia and phoria led to development of the Quereau-Putnam Tropophorometer.[2] This instrument is without inherent error. Its targets move spherically about each eye's center of rotation, and actual distance, both far and near, is used in fixation, instead of the illusion of distance. These features are combined in an instrument designed to be used with the cover test for the best possible elimination of the tendency toward fusion.

The human error of manipulation is present in adjusting the head and the instrument to their proper positions. With such an instrument the interpupillary distance can be adjusted to within 1 mm. Vertical adjustment can be made to within 1 mm., and forward or backward adjustment, to within 2 mm. With ordinary care maximum deviation of the sphere center from the center of rotation of the eye will not exceed 3 mm. and will average under 2 mm. This is a source of decentering error too small to affect significantly any measurement even at the nearest fixation distance that may be desired, being

2. Quereau, J. V., and Putnam, O. A.: Quereau-Putnam Tropophorometer, Arch. Ophth. **33**:28 (Jan.) 1945.

under 1 per cent at a fixation distance of 12 inches (30.48 cm.). Scales can be read to 0.25°, and the instrument affords a means of knowing precisely how far into the fields of action of the oblique and rectus muscles each measurement is made.

CONCLUSION

A knowledge of the degree of precision and of error inherent in various methods of measuring squint and phoria discussed in this paper and of the means of compensating for them will increase the accuracy of diagnosis of anomalies of the extraocular muscles. These errors and the means of compensating for them may be summarized as follows:

1. The error in effectivity in prism measurements is the angle formed by a line from a fixation point to the center of rotation of the eye and a line from the fixation point to the outer surface of the prism at a point such that after refraction it will coincide with the visual line of the eye.

For small measurements, the error in effectivity may be sufficiently minimized by (1) holding the muscle light at least 16 inches (40.6 cm.) away from the patient and (2) holding the prism as close to the eye as possible.

For large measurements (25△ and over), the error in effectivity may be compensated for by subtracting the error in effectivity from the measured deviation in which

$$\% \text{ error} = 100 \frac{\text{distance from center of eye to outer face of prism}}{\text{distance from center of eye to fixated object}}$$

2. False hyperphoria in the oblique directions is measured when either exophoria or esophoria exists and the measurement is made at near fixation distance.

(*a*) For prisms, the error in diagnosis due to false hyperphoria can be avoided by (1) rotating the laterally measuring prism slightly around its horizontal axis (*X*, fig. 4) until its near (inner) surface is perpendicular to the plane of fixation (movement *1*, fig. 5 *C* and *D*), then (2) rotating the tilted prism around its vertical axis (*Z*, fig. 4) until the near surface is perpendicular to the portion of the visual line from eye to prism (movement *2*, fig. 5 *C* and *D*).

(*b*) The Maddox rod should be tilted exactly as for the near surface of a prism which is correcting the lateral deviation, as previously described. When this is done, the line formed by the Maddox rod will not appear horizontal (or level) to the patient. The patient will see the line tilted so that its nasal end is lower than the temporal end when measurements are made below the horizontal plane, and its nasal end is higher than the temporal end when measurements are made above the horizontal plane.

(*c*) The red glass cannot be held so as to compensate for the false hyperphoria in oblique directions. It can be used accurately only when no esophoria or exophoria exists, for then there will be no false hyperphoria. The red glass has accuracy in the horizontal and vertical planes but not in the oblique directions.

3. Variations in the size of the prism diopter unit need not be considered a serious source of error. This is because the practice of employing two prisms of moderate size and adding their dioptric power, instead of using one very strong prism, effectively minimizes the error due to the variation in the value of the prism diopter unit, which is serious only in large prisms.

4. Variation in prism and target distance from one examination to another is a source of error unless a record is kept of the distances used and these distances are kept constant.

5. Change of prism strength with rotation may be minimized by strict observance of the Prentice position or by erring on the side of the split position.[1]

6. Amblyoscopes have a large decentering error when set for near point measurement unless their vertical axes pass through the centers of rotation of the eyes.

7. Perimeters and the Hirschberg reflex method are useful only for gross measurement of lateral tropia.

Dr. LeGrand H. Hardy made helpful suggestions and corrections in the preparation of this manuscript.

206 North Fifth Street (Dr. Quereau).

CLINICAL USE OF OPHTHALMIC PRISMS (METRIC)

LE GRAND H. HARDY, M.D.
NEW YORK

In a previous report [1] the origins and developments of the present systems of numbering ophthalmic prisms were discussed, and attention was called to three important facts:

1. The power of prisms frequently departs unjustifiably from reasonable manufacturing standards.
2. Different units of power are used, but the unit used is rarely indicated on the label.
3. Enormous errors are introduced in using strong prisms unless careful precautions are taken respecting the position in which the prism is held and the unit used.

Both the Dennett [2] system of utilizing the prism centrad (∇) as a unit and the Prentice system [3] of utilizing the prism diopter ($\triangle$) as a unit require that all refractive effect must take place at one surface. This condition is violated more frequently than it is observed in clinical practice. I have watched many ophthalmologists, teachers as well as students, in making their measurements of squint, and the usual procedure is to hold the prism between thumb and forefinger in such a position that the altitude of the prism is roughly in line with the forefinger, and it is this line which is held approximately normal, or at right angles, to the optic axis of the deviating eye (X axis, fig. 10).

To simplify the discussion, I shall call this position the "split position" (the visual line of the eye is normal to a line splitting the apex angle of the prism), and the purpose of this discussion is to analyze the errors introduced into measurements by improper positioning of the metric prism.

Accepting for the moment the prism diopter as the operational unit of strength of the prism and ignoring the Prentice postulate that all effect must take place at one refractive surface, one may consider how deviations from this position affect the apparent power of the prism.

Seven fixed positions immediately become apparent.

1. The position of maximal deviation ($e = 90°$), in which the emergent ray just grazes the surface of the prism.
2. The position of the maximal deviation ($i = 90°$), corresponding to position 1, in which the entering ray just grazes the surface.
3. The position of minimal deviation, in which the prism exerts its least effect. In this position the ray inside the prism travels at right angles to a line bisecting the apex angle; i. e., in a symmetric prism the ray inside travels parallel to the base ($e = i$).
4. The Prentice position, in which the entering ray meets the first surface of the prism at right angles ($i = 0°$).
5. The Prentice position, corresponding to position 4, in which the path of the ray is reversed. In this position the emerging ray is perpendicular to the last surface ($e = 0°$).
6. The "split position," in which the entering ray outside the prism is traveling on a line at right angles to the line bisecting the apex angle. This is the position in which prisms are usually observed to be held ($i = \frac{a}{2}$).
7. The reverse of the split position, in which $e = \frac{a}{2}$.

Measurements of twenty sets of prisms were made in all these positions and checked against calculated values, to produce the accompanying charts and table.

The following formulas were derived for the powers of deviation (δ) of various prisms held in these positions. All formulas were derived directly from Snell's law ($n \sin i = n' \sin r$), using the index of refraction of glass as $n' = 1.523$. This index, by reverse calculation, was made a basis for checking on the accuracy of measurements.

The formula for maximal deviation ($\delta\ max$) is

$$\delta\ max = \sin^{-1} n' \sin (a - C) + 90 - a \quad (1)$$

The formula for minimal deviation ($\delta\ min$) is

$$\delta\ min = 2\ [\sin^{-1} (n' \sin \tfrac{a}{2})] - a \quad (2)$$

From the Knapp Memorial Laboratories, Institute of Ophthalmology, Presbyterian Hospital.

1. Hardy, L. H.; Chace, R. R., and Wheeler, M.: Ophthalmic Prisms: Corrective and Metric, Arch. Ophth. **33**:381 (May) 1945.
2. Dennett, W. S.: A New Method of Numbering Prisms, Tr. Am. Ophth. Soc. **5**:422, 1889.
3. Prentice, C. F.: A Metric System of Numbering and Measuring Prisms, Arch. Ophth. **19**:64 and 128, 1890.

The formula for deviation in the Prentice position (δ *prent*) is

$$\delta \textit{ prent} = \sin^{-1} n' \sin a - a \qquad (3)$$

The formula for deviation in the split position (δ *split*) is

$$\delta \textit{ split} = \sin^{-1}\left\{ n' \sin\left[a - \sin^{-1}\left(\frac{\sin\frac{a}{2}}{n'}\right)\right]\right\} - \frac{a}{2} \qquad (4)$$

Where δ = angle of deviation, in degrees
a = apex angle of prism
C = critical angle of glass with index 1.523 = 41° 2′

All of these formulas may be derived from elementary trigonometric procedures, but since I have noticed that most ophthalmologists are averse to analyzing mathematical formulas, I shall give the elementary, step by step derivation of only the last, and new, position.

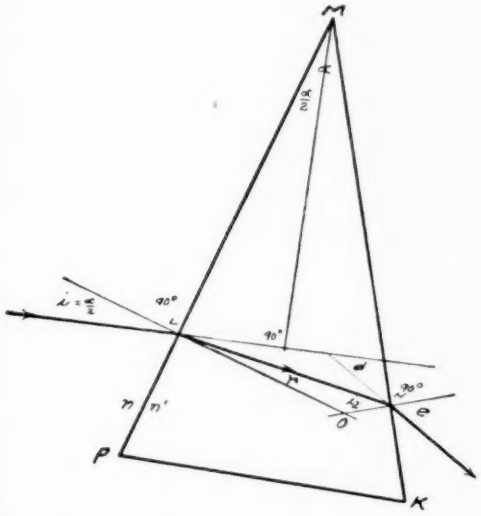

Fig. 1.—The split position of a prism, the position usually used in measuring squint.

In the prism PMK (fig. 1) one needs only to know the values for i, r, i_2 and e to get the value for δ, which is expressed in the general prism equation:

$$\delta = i + e - a \qquad (5)$$

Now $i = \frac{a}{2}$
since the sides of i are perpendicular to the sides of $\frac{a}{2}$

From Snell's law $n \sin i = n' \sin r$
and since $n = 1$ and $i = \frac{a}{2}$

$$\sin\tfrac{a}{2} = n' \sin r, \text{ or } \sin r = \frac{\sin\frac{a}{2}}{n'}, \text{ or}$$

$$r = \sin^{-1}\left(\frac{\sin\frac{a}{2}}{n'}\right) \qquad (6)$$

To obtain i_2:
The sum of the angles in the quadrilateral $LMNO = 360° \cdot L = 90°$ and $N = 90°$
Therefore $a + O = 180°$
and $r + O + i_2 = 180°$ (sum of internal angles of triangle)
Hence $r + O + i_2 = a + O$
Hence $i_2 = a - r$
And, substituting the value for r from (6)

$$i_2 = a - \sin^{-1}\left(\frac{\sin\frac{a}{2}}{n'}\right) \qquad (7)$$

To obtain e:

$$n \sin e = n' \sin i_2$$

and since $n = 1$

$$\sin e = n' \sin i_2, \text{ or } e = \sin^{-1} n' \sin i_2$$
$$e = \sin^{-1} n' \sin i_2 \qquad (8)$$

To obtain δ:
Since $\delta = i + e - a$ (equation 5)
and $i = \frac{a}{2}$

$$\delta = \tfrac{a}{2} + e - a = e - \tfrac{a}{2}$$
$$\delta = e - \tfrac{a}{2}$$

And since $e = \sin^{-1} n' \sin i_2$
and $i_2 = a - r$

$$e = \sin^{-1}\left[n' \sin (a - r)\right]$$

Substituting (6) for r

$$e = \sin^{-1}\left\{ n' \sin\left[a - \sin^{-1}\left(\frac{\sin\frac{a}{2}}{n'}\right)\right]\right\}$$

From $\delta = e - \frac{a}{2}$
substituting value for e, just derived

$$\delta = \sin^{-1}\left\{ n' \sin\left[a - \sin^{-1}\left(\frac{\sin\frac{a}{2}}{n'}\right)\right]\right\} - \frac{a}{2}$$

which is equation 4 for δ *split*.

The accompanying table gives the values for the apex angle (a) of prisms from 1 △ to the theoretic limit (115 △) of prisms in the Prentice position.

From the table the value for the apex angle (a) corresponding to any value for the prism (△) may be taken to be used in formulas 1 to 4.

Figures 2 to 7 inclusive illustrate deviations produced by a 40 △ prism ($n' = 1.523$) when held in the various positions. The data from the table are illustrated in figure 8 as a dotted line. From this graph it may be seen that, whereas up to about 20° the apex angle (a) and the deviations produced with the prism held in the split position and in the Prentice position are in substantial agreement, beyond this point they diverge widely. The power in the Prentice position departs from the power in the position of minimal deviation and with increasing rapidity approaches the maximal power. The power in

the split position is much less aberrant, but it, too, follows the inevitable course, and all curves reach a common point (at $a = 81° 32'$) where the deviation becomes infinity.

How does the deviation vary with respect to the position, that is, to the angle of incidence? It has been found possible to develop a formula for this,[4] which is:

$$\delta = \cos^{-1}\left\| n' \cos\left[a + \cos^{-1}\left\{ \frac{\cos(90 - i)}{n'} \right\} \right] \right\| - (90 - i + a) \qquad (9)$$

Apex Angle (a) for Prisms 1 Δ to 115 Δ Calculated *

Apex Angle (a) Degree (°)	Min. (′)	Prism (Δ)
1	06	1
2	11	2
3	17	3
4	21	4
5	29	5
6	31	6
7	35	7
8	36	8
9	40	9
10	41	10
11	42	11
12	39	12
13	38	13
14	35	14
15	32	15
16	25	16
17	20	17
18	11	18
19	01	19
19	54	20
23	40	25
26	58	30
29	42	35
31	58	40
33	53	45
35	26	50
37	42	60
39	09	70
40	06	80
40	37	90
40	55	100
41	01	110
41	02	115

* This table illustrates the commonly taught fact that there is little difference between the apex angles, in degrees, and the dioptric strength, in prism diopters, up to about 20 Δ, but that beyond this point the difference increases with great rapidity.

Since the critical angle for glass with an index of refraction (n') of 1.523 is 41° 02′, an apex angle of this dimension represents the strongest that can be manufactured and marked in prism diopters.

If one ignores the Prentice position, the strongest possible prism would have double the critical angle of glass as its apex angle; it would deviate a ray of light through more than a right angle (97° 56′) and would hence have what might be considered as a minus power of —717.6 Δ.

From this formula has been calculated a family of curves (one curve for each prism) showing the apparent effect produced as the prism was rotated from the position at which $i = 90°$ to the position at which $e = 90°$. Since the concepts considered here are predominantly concerned with prism diopters, the values for δ (given in the formula as degrees, or $\delta°$) have been transformed (invalidly) into prism diopters ($\delta\Delta$).

$$\delta\Delta = 100 \tan \delta° \qquad (10)$$

The index of refraction of glass is considered throughout as $n' = 1.523$. The value for i is assigned. The value for a is taken from the table. The value of δ, expressed in degrees ($\delta°$), is calculated and converted into prism diopters ($\delta\Delta$) by formula 10.

The results are arresting and instructive. They can better be seen in graph form than in a table, since fifteen pages of tabular material can be presented in one graph. Figure 9 presents the data derived from the foregoing calculations.

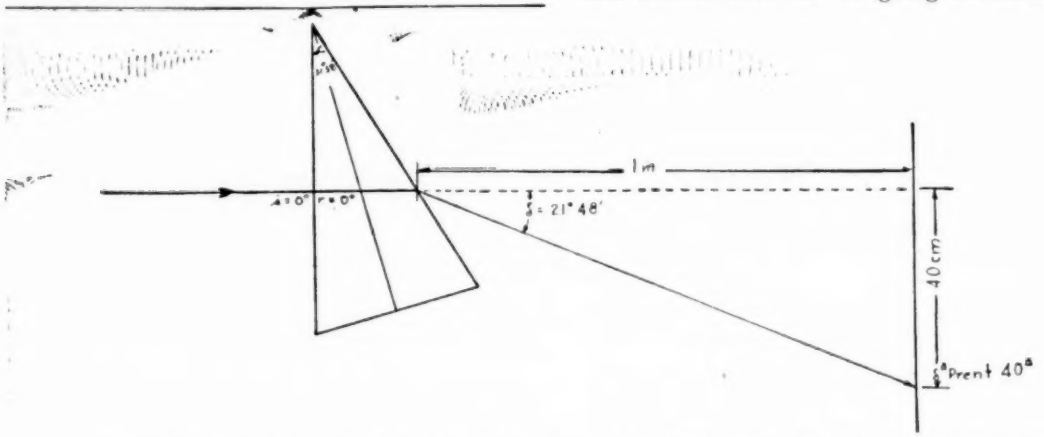

Fig. 2.—Deviation produced by a 40 Δ prism of glass ($n' = 1.523$) when held in the Prentice position, in which $i = 0°$.

EFFECTS OF ROTATING MEASURING PRISMS

It is obvious that the measurements and calculations so far recorded have yielded deviations produced in seven positions which represent only points in a continuous curve. That is, the deviation produced by any prism will vary continuously from one maximum ($i = 90°$) down to the minimum deviation and back up through the deviations for the split position and the Prentice position to a second, and equal, maximum deviation, where $e = 90°$.

Each curve represents the effects produced by a single prism. The left hand ordinate ($i = +90°$) indicates the maximal effect produced when the incident ray grazes. The heavy upward curving line represents the effect produced in the position of minimal deviation; the light similarly curving line shows the effect produced in the split position; the straight vertical dotted line at $i = 0°$ marks the effect produced

4. Dr. Paul Boeder helped in developing this formula and checked all the other formulas.

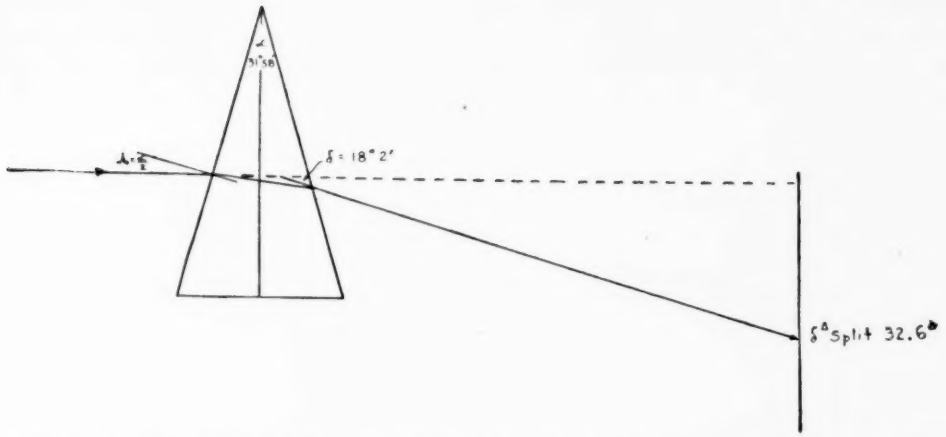

Fig. 3.—Deviation produced (invalidly recorded in prism diopters) by the same 40 △ prism (apex angle, 31° 58′) when held in the split position, in which $i = \frac{a}{2}$

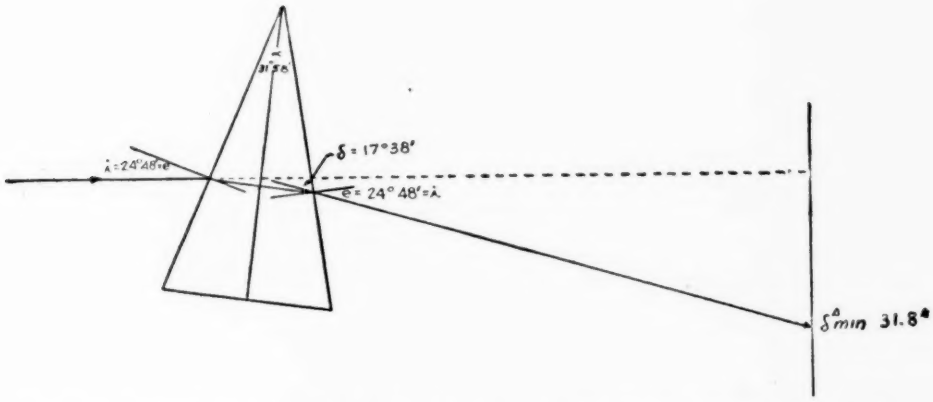

Fig. 4.—Deviation produced by a 40 △ prism (31° 58′ apex angle) in the position of minimal deviation, in which $i = e$.

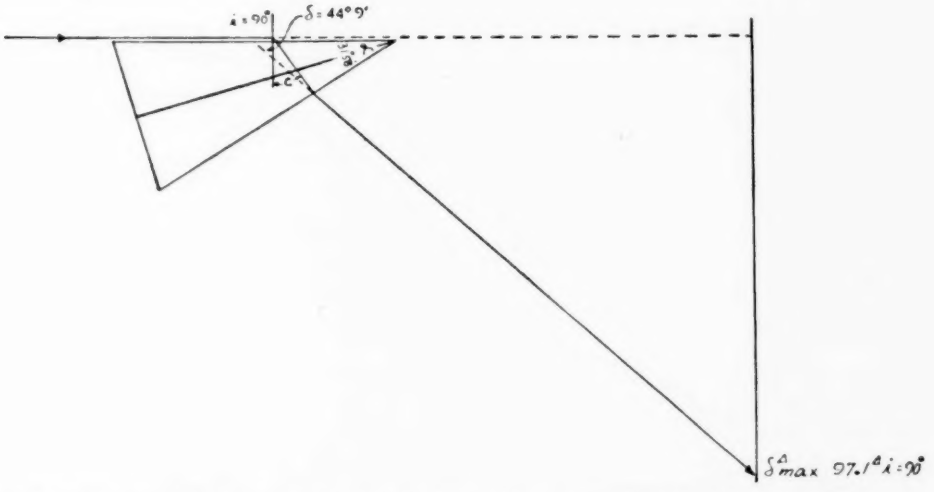

Fig. 5.—Deviation produced by a 40 △ prism in the position of maximal deviation ($i = 90°$).

In this graph, and in that shown in figure 6, C indicates the critical angle (41° 2′) for glass with a refraction index (n') of 1.523.

in the Prentice position, and the right hand boundary of the curve shows the maximal effect when $e = 90°$ (emergent ray grazes).

Note that whereas a 1 △ prism has practically the same effect when held in the Prentice, position, in the split position and in the position of minimal deviation, it can be made to produce an effect of 19.5 △ if improperly positioned. Practically, this is not a serious error, since there is little or no chance of such mishandling.

A 20 △ prism has an effect of 19 △ in the position of minimal deviation and almost the same power in the split position, but it can be given a power of almost 75 △ by improper positioning. If it is turned only 30°, so that the incident ray approaches from the apex side of the normal, it will exert a power of over 44 △.

Metric prisms used for measuring squint usually come in sets of strengths up to 50 △ Note how dangerous the Prentice position is

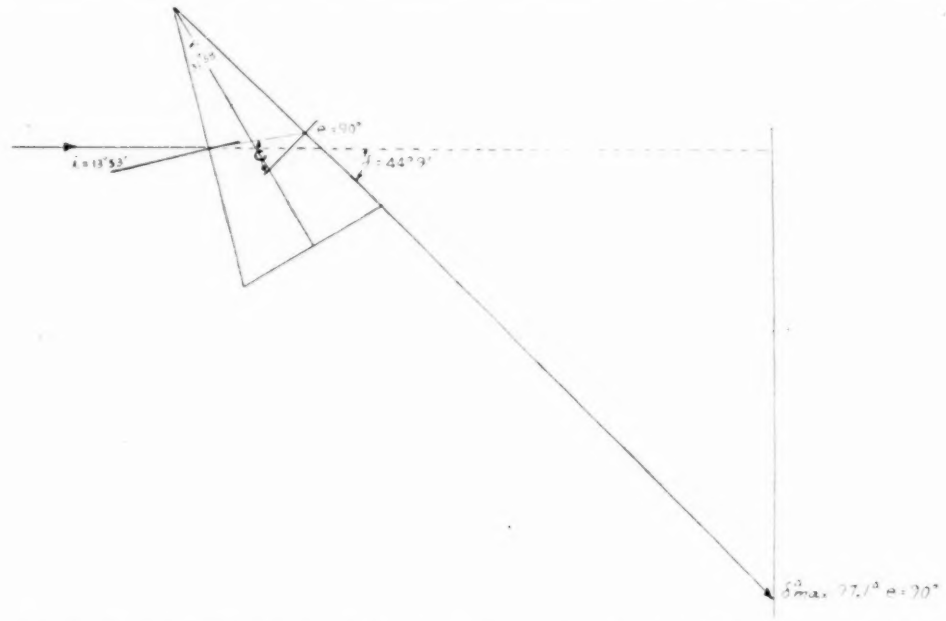

Fig. 6.—Deviation (97 △) of a 40 △ prism in the position of maximal deviation ($e = 90°$).

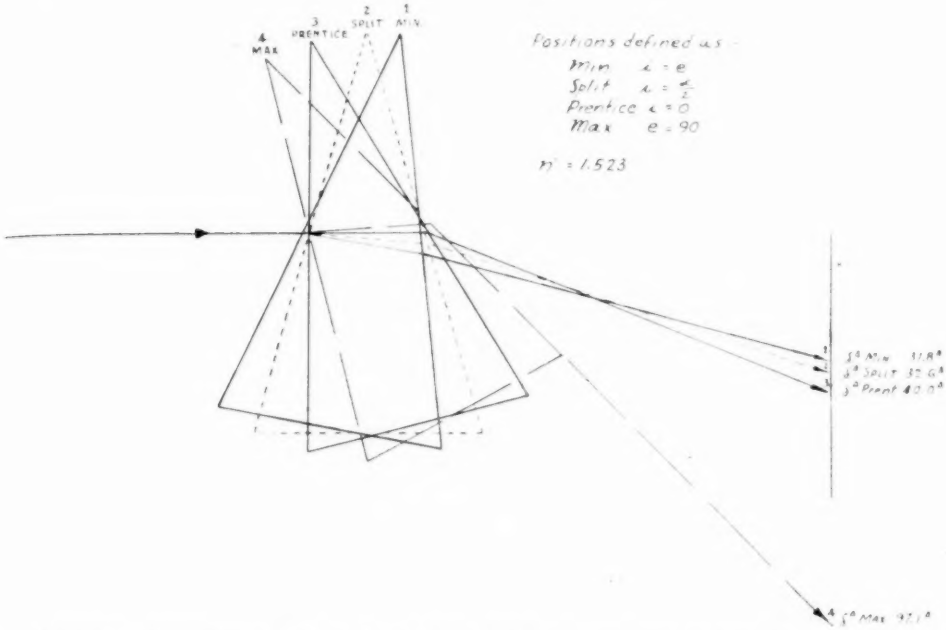

Fig. 7.—Composite illustration depicting the different deviations produced by the same 40 △ prism as it is held in various positions relative to the entering ray.

at this value. A 50 △ prism has a minimal deviation of 36.46 △, a deviation of 37.65 △ in the split position but may be given a maximal deviation of 103.61 △ with improper holding, and it needs to be rotated less than 9° to produce this effect. This is an important fact which is not widely known and seldom guarded against, and it partly explains why many ophthalmologists stop using prisms at about 40 △ and rely on guesswork beyond that point.

Even at 40 △ a valuable lesson is to be drawn from figure 9. It has been seen in figures 2 to 8 how a 40 △ prism behaves in effect. To rotate a 40 △ prism 10° toward the apex increases its effect to 57 △, introducing an error of 17 △. If, however, two 20 △ prisms were utilized, one over each eye, and the same error committed with each, the total effect would amount to only 2 × 2.7, or 5.4 △. It is thus obvious that in measuring the higher degrees of

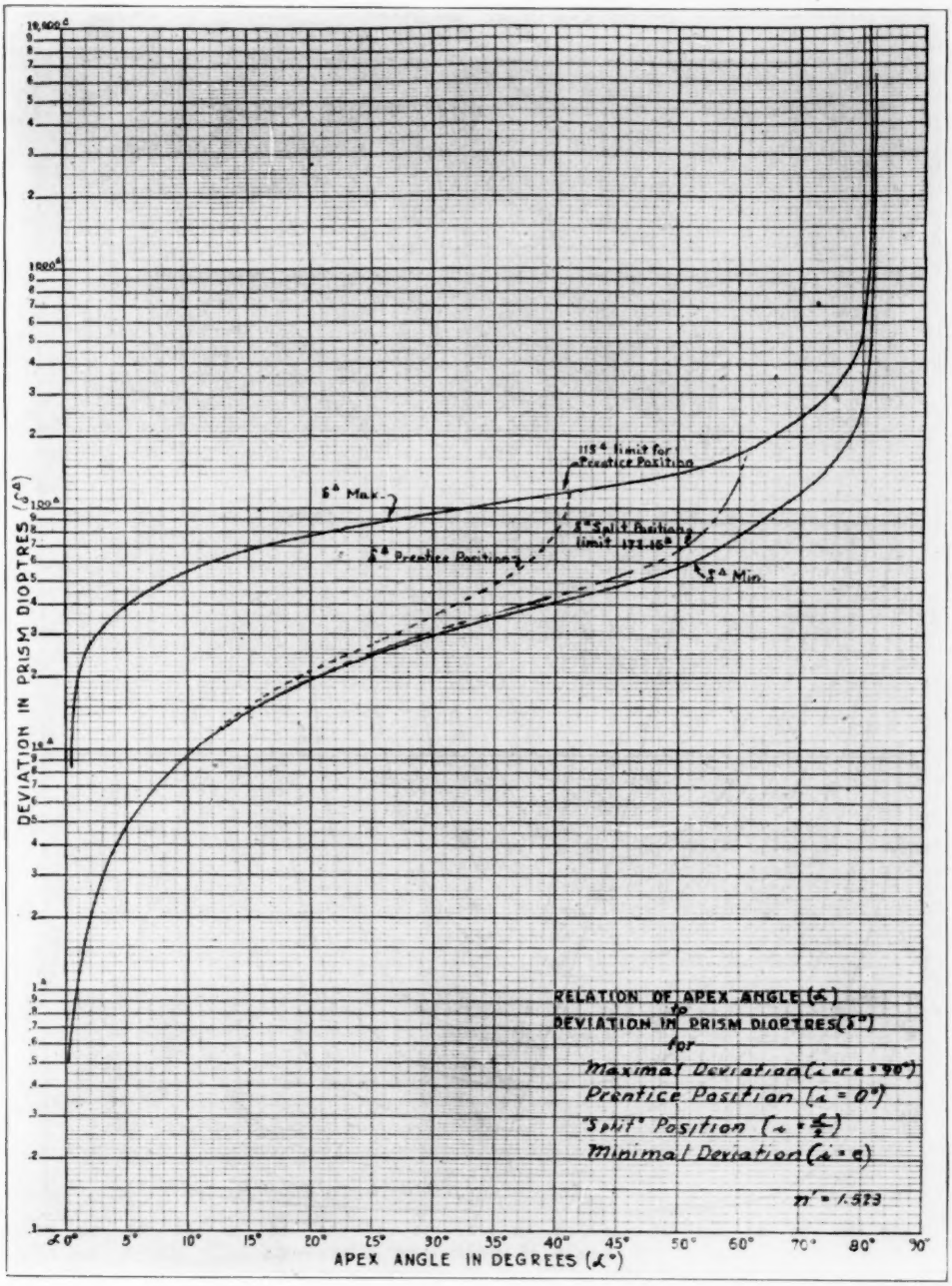

Fig. 8.—Relation of apex angle of prisms to deviation in prism diopters.

squint, less error is introduced when the prism strength is divided between the two eyes.

It is apparent that maximal errors will not often occur except when high power prisms are carelessly used. It is equally obvious from figure 9 that the position of minimal deviation is the safest position to use in safeguarding against error and that the Prentice position occupies a dangerous area of the curves. The position of minimal deviation was the one earnestly advocated by Jackson [5] many years ago; but since it is a variable position, it has found scant support.

The split position is the one which is intuitively widely used, and it is good fortune that it deviates from the Prentice position toward the position of minimal deviation. While it is not the ideal, it represents an escape from the dangers of the Prentice position and an approach to the more scientific and less dangerous position of minimal deviation. It is the position in which, perforce, many instruments, such as rotary

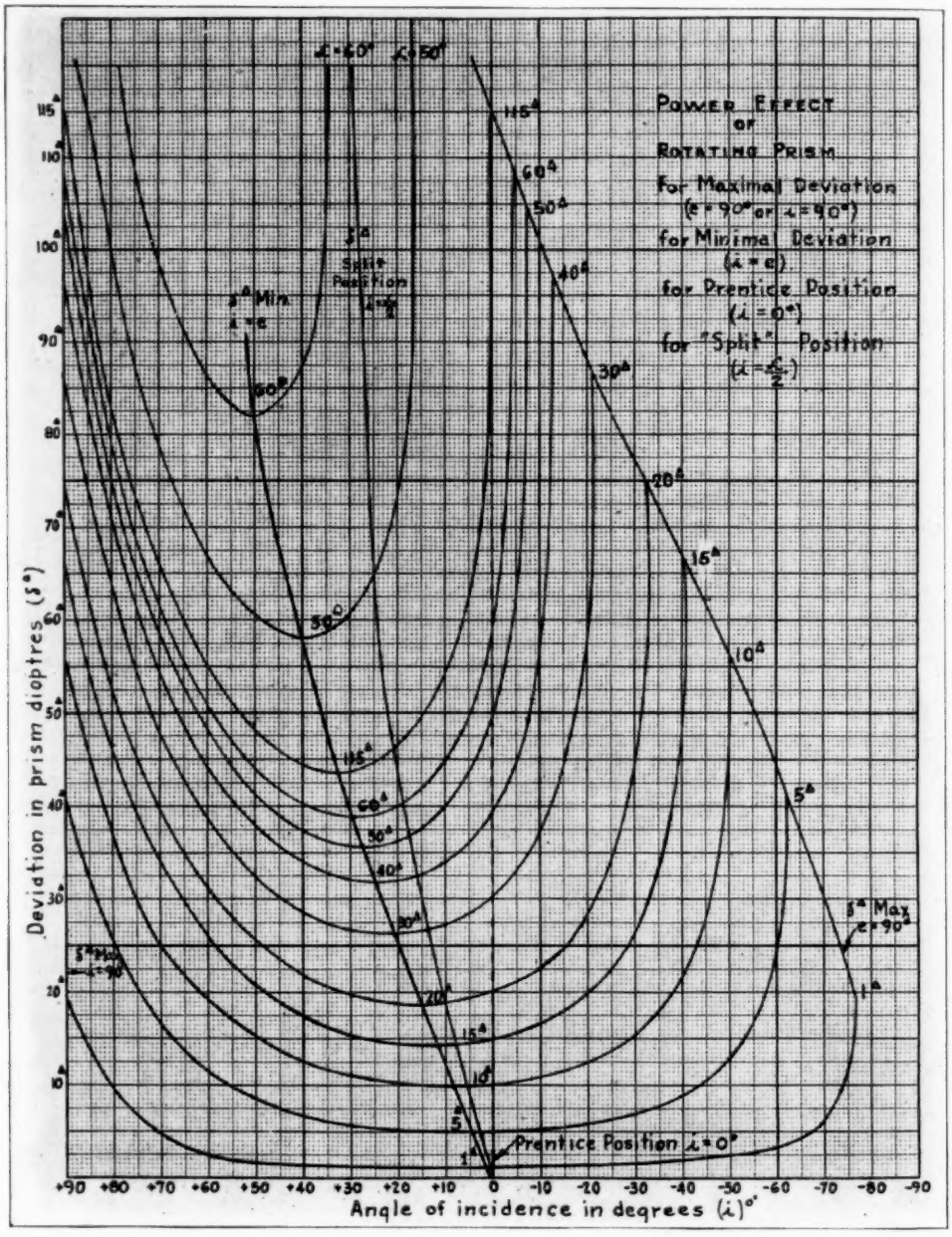
Power Effect of Rotating Prism
For Maximal Deviation (ε = 90° or i = 90°)
for Minimal Deviation (i = ε)
for Prentice Position (i = 0°)
for "Split" Position (i = ε/2)
Deviation in prism dioptres (δ°)
Angle of incidence in degrees (i)°
Prentice Position i = 0°
+90 +80 +70 +60 +50 +40 +30 +20 +10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90

Fig. 9.—The power effect of rotating prisms.

5. Jackson, E.: The Designation of Prisms by the Angular Deviation They Cause Instead of by the Refracting Angle, Tr. Internat. M. Cong. (Sect. 11, Ophth.) **3**:785, 1887.

prisms in phorometers and similar instruments, must mechanically be set.

The changes in power of a prism due to the holding position have been discussed from only one point of view; i. e., the changes which result when the prism has been rotated about its major axis from the Prentice position. The major axis may be described as the axis joining the geometric centers of the plane parallel sides of the prism. It is a line bisecting the apex angle and lying parallel to the apex of the prism (*Z* axis, fig. 10).

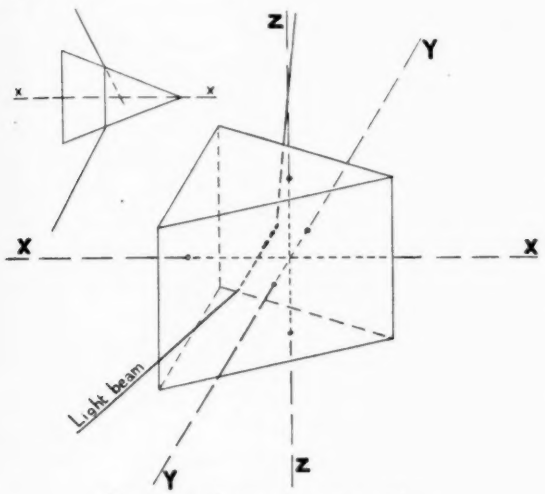

Fig. 10.—Major axes of a prism.

There are two other axes of a prism. One, the face axis (or fore and aft axis), is a line joining the centers of the inclined faces of the prism. (This line would be parallel to the base in a symmetric prism [*Y* axis, fig. 10].) It is the line describing the path of the internal light ray when the prism is held in the position of minimal deviation. Rotating the prism about this axis would convert a horizontal deviation into a vertical deviation; i. e., it would change the position of the prism from base horizontal to base down or base up. With increasing rotation the amount of deviation produced by the prism in the horizontal meridian is reduced, while an increasing vertical component is added.

Rotating the prism about the third axis, which bisects the apex angle and is equidistant from the parallel surfaces (*X* axis, fig. 10), results in spatial distortion and some change in power. The path of the ray inside the prism is prolonged. The geometric principles involved in this change have been described by Southall.

Finally, the distance from the eye at which the prism is held will change its effectivity. The farther from the eye the prism is held, the less is its effective deviational power. This is analogous to the change in effectivity produced by changing the distance from the eye in which the lens is held.

SUMMARY

The clinical use of ophthalmic prisms for measuring deviations of the eyes involves little known but serious dangers of committing error, particularly in the higher powers.

The units of prism strength are not usually marked on the prisms; and since several units are in use, this dereliction should be remedied.

Great care should be used in positioning metric prisms to avoid error.

If errors in positioning are made, it is much safer to err on the side of inclining the prism toward the position of minimum deviation than away from it.

The split position is a natural and intuitive manner of holding metric prisms which tends to avoid the dangers of the Prentice position.

In measuring high degrees of deviation, it is much safer to divide the prisms, holding approximately half the amount over each eye.

23 East Seventy-Ninth Street.

CATARACT AND OTHER CONGENITAL DEFECTS IN INFANTS FOLLOWING RUBELLA IN THE MOTHER

JOHN C. LONG, M.D., AND RALPH W. DANIELSON, M.D.
DENVER

Recent observations, particularly from Australia, seem to indicate that rubella during early pregnancy may lead to multiple serious congenital defects in the offspring. This was first noted in 1941 by Gregg [1] following a severe Australian epidemic of German measles. It is thought that crowding and troop movements may have made possible the rapid transfer of the virus from one person to another, and thus not only may have spread the epidemic but also may have caused some change in the virus.

Gregg described 78 cases of congenital cataract, 20 examined personally and the remainder reported to him by his colleagues. In 68 of these cases there was a definite history of German measles in the pregnant mother. Cardiac lesions were present in at least 44 of the 78 infants. A research team sponsored by the National Health and Medical Research Council of Australia, consisting of Drs. Swan, Tostevin, Moore, Mayo and Black, carried out a widespread investigation by examination and questionnaire, reporting their results in two papers.[2] They found that of 61 mothers who contracted German measles during pregnancy, 41 bore children with congenital defects. These babies were abnormally light in weight even if born at term. There were 15 cases of cataract, 1 of buphthalmos, 3 of microphthalmos, 12 of deaf-mutism, 21 of cardiac abnormalities, at least 15 cases of some degree of microcephaly, and 1 case each of hypospadias, obliteration of the bile ducts and talipes equinovarus. Mental deficiency was probably present in several children. Swan and his associates are under the impression that the type of defect is somewhat determined by the stage of pregnancy at which rubella is contracted. Thus the average duration of pregnancy in the mothers whose offspring had cataract was one and four-tenths months while the duration in those whose infants were deaf-mutes was two and three tenths months. The authors stated that "on the available evidence, when a woman contracts rubella within the first two months of pregnancy it would appear that the chances of her giving birth to a congenitally defective child are in the region of 100 per cent, and if she contracts rubella in the third month they are about 50 per cent." Evans,[3] after studying some of the cases reported by Swan and his associates, stated that of 34 babies whose mothers suffered during pregnancy from rubella, 23 exhibited congenital dental abnormalities. These dental defects consisted of retardation of eruption, enamel hypoplasia and dental caries.

Reese,[4] in 1944, published the first American report on the association between German measles and congenital defects, with observations on 3 New York infants. All had cataracts and congenital heart defects. Rones,[5] from Washington, D. C., reported the occurrence of cataract in 2 infants whose mothers had contracted rubella during the second month of pregnancy and 1 case of congenital glaucoma in an infant whose mother had become infected during the third month. Erickson [6] described 11 California infants with congenital cataract, 9 of whom also had defects of the heart.

These reports, from widely scattered sources, point out the necessity for further observations on what appears to be one of the important factors in the development of several congenital defects. We shall describe 6 cases that we have personally observed.

1. Gregg, N. M.: Congenital Cataract Following German Measles in Mother, Tr. Ophth. Soc. Australia **3**:35-46, 1941.

2. (*a*) Swan, C.; Tostevin, A. L.; Moore, B.; Mayo, H., and Black, G. H. B.: Congenital Defects in Infants Following Infectious Diseases During Pregnancy, M. J. Australia **2**:201-220 (Sept. 11) 1943. (*b*) Swan, C.; Tostevin, A. L.; Mayo, H., and Black, G. H. B.: Further Observations on Congenital Defects in Infants Following Infectious Diseases During Pregnancy, with Special Reference to Rubella, ibid. **1**:409-413 (May 6) 1944.

3. Evans, M. W.: Congenital Dental Defects in Infants Subsequent to Maternal Rubella During Pregnancy, M. J. Australia **2**:225-228 (Sept. 2) 1944.

4. Reese, A. B.: Congenital Cataract and Other Anomalies Following German Measles in the Mother, Am. J. Ophth. **27**:483-487 (May) 1944.

5. Rones, B.: The Relationship of German Measles During Pregnancy to Congenital Ocular Defects, M. Ann. District of Columbia **13**:285-287 (Aug.) 1944.

6. Erickson, C. A.: Rubella Early in Pregnancy Causing Congenital Malformations of Eyes and Heart, J. Pediat. **25**:281-283 (Oct.) 1944.

REPORT OF CASES

CASE 1 (J. R. N.).—The mother contracted rubella when three or four weeks pregnant during a mild epidemic in St. Louis. The disease apparently was acquired from a daughter, who in turn had been exposed to a case of German measles. The disease in the mother consisted of sore throat, cervical adenopathy and a marked eruption on the face with some lesions on the arms. She was not confined to bed and did not consult a physician. The mother stated that she had previously had rubella when 7 or 8 years of age. She had 1 healthy daughter, aged 3. There was no family history of congenital eye or heart defects.

The patient, a boy, was born on Dec. 31, 1943, weighing 4 pounds, 4 ounces (1,927.76 Gm.). Dr. H. Rommel Hildreth saw the baby shortly after birth and made a diagnosis of congenital cataract of the right eye with slight microphthalmos. Our examination a year later confirmed these findings. The baby fixed on a light and showed an interest in the environment. The right eye was convergent to a variable amount, approximately 20 to 25 degrees. The right eyeball, including the cornea, was smaller than the left. The pupils were approximately equal in size and both reacted briskly to light. Both pupils dilated well with homatropine hydrobromide and paredrine hydrobromide. The right lens was diffusely hazy with a sharply demarcated dense central opacity. A dull fundus reflex, but no details, could be seen through the periphery of the lens. The anterior segment of the left eye, including the lens, seemed normal. The vitreous was hazy, and there were numerous moderately large opacities. The disk seemed abnormally pale. The entire posterior pole showed a diffuse mottled pigmentation as though from a mild chorioretinitis. The infant accurately fixed the ophthalmoscope light on the macula. Examination, including tonometry, under a general anesthetic was contemplated but not done owing to a severe congenital defect of the heart, thought to be a patent interventricular septum.

CASE 2 (K. A.).—The mother, aged 44, had German measles probably the first month or six weeks of pregnancy. A daughter acquired the disease during an epidemic at Kremmling, Colo., and communicated the infection to the mother and to another daughter. The mother had not previously had rubella. She was not very sick with the German measles but did have considerable cervical adenopathy, and about a week later varicose veins and pulmonary disturbance developed. The mother had previously had seven normal children. There was no family history of any congenital defect.

The patient, a boy, was born on March 9, 1943, weighing 5 pounds 15 ounces (6,803.88 Gm.). There was a definite feeding problem, and he had several attacks of cyanosis. General examination revealed a congenital lesion of the heart, probably a septal defect. On April 12, 1943, the right cornea seemed slightly steamy and the pupil was dilated and fixed to light. The right fundus could be seen, showing some diffuse mild pigmentary disturbance. The left eye was distinctly smaller than the right, and the lens was cataractous. The entire lens was partially opaque, but the opacity in the pupillary zone was definitely more dense. The left pupil reacted normally to light. It was thought that the right eye was probably glaucomatous; so a salt of pilocarpine was prescribed. On July 16, 1943, the general condition having improved sufficiently to permit it, examination was carried out under general anesthesia. The intraocular pressure was 17 mm. in the right eye and 20 mm. in the left eye (Gradle-Schiøtz). The right cornea had lost its steamy appearance, and both pupils reacted briskly to light. The mild, diffuse disturbance of the chorioretinal pigment of the right eye was confirmed. The intraocular pressure has since been rechecked and found normal. The boy is alert and has developed well. He apparently has good vision in the right eye.

CASE 3 (G. B. B.).—The mother had German measles when four to six weeks pregnant, while living in Cripple Creek, Colo. The rash first appeared on the abdomen, later spreading to the chest and face. Slight cervical lymphadenopathy was present. She was not confined to bed but a physician was called, who confirmed the diagnosis of rubella. This was the first pregnancy. There was no family history of any congenital defect.

The baby, a boy, was born at term, on Dec. 31, 1942, weighing 6 pounds 10 ounces (3,005.05 Gm.). Both eyeballs were abnormally small on gross inspection. Bilateral cataracts were observed shortly after birth. The entire pupillary area was opaque in both eyes. The pupils were small and did not dilate well with mydriatics. A discission was done on the right eye on Feb. 16, 1943, but a clear pupil was not obtained. On Sept. 28, 1943, a discission was done on the left eye, a vertical incision being made through a soft membranous cataract. A clear opening was immediately apparent. A second discission was done on the right eye on Sept. 26, 1944. The baby has a congenital heart lesion, probably a septal defect, and bilateral cryptorchid testes. General development has been retarded, and the child has been slow in walking and talking.

CASE 4 (R. L. T.).—The mother, aged 18 years, contracted German measles from a daughter when about three weeks pregnant, while living in Loveland, Colo. A sister also became infected at the same time. The mother had a generalized rash but was not confined to bed. The diagnosis of rubella was confirmed by a physician. The mother stated that she probably had rubella in childhood. There was one other child, aged 3 years, in good health. There was no family history of any congenital defect.

The baby, a boy, was born at term on Dec. 11, 1942, weighing 4½ pounds (2,041.16 Gm.). He did not void until catheterized but has had no further urinary difficulty. There was a slight valgus deformity of the right foot. The heart was definitely abnormal, the heart sounds being largely obliterated by a loud murmur. He presented a feeding problem. On Jan. 25, 1945 an examination was made under general anesthetic and a discission of a cataract of the right eye was done. The right eye was definitely smaller than the left. The right cornea measured 9.7 mm. in the horizontal meridian while the left measured 11 mm. The entire right lens was hazy, but the central zone showed a dense, sharply delimited opacity. The left eye seemed normal except for a diffuse pigmented mottling of the fundus with the greatest irregularity of pigmentation in and temporal to the macular region. Since the discission the lens material has shown little tendency to absorb.

CASE 5 (G. C. K.).—The mother, aged 31, had German measles when about four weeks pregnant, while living in Denver. The illness began with a slight sore throat and malaise followed by an eruption of the arms, face and torso. The eruption lasted for three days, during which time the mother remained in bed but was not especially ill. There was no family history of any congenital defect.

The baby, a girl, was born on Dec. 8, 1944, weighing 6 pounds 5 ounces (2,863.3 Gm.). She was cyanotic at times and was difficult to feed. Roentgenograms of the chest showed a transverse enlargement of the heart. Clinical signs were suggestive of an interventricular septal defect. When examined on Feb. 12, 1945, the baby seemed to be in fair general condition. Both eyes showed a mucopurulent secretion, and this material could be expressed from both tear sacs. Both eyes were abnormally small, especially the right. The pupils reacted sluggishly to light and dilated poorly with homatropine and paredrine hydrobromide. Both lenses were densely opaque with a suggestion that the periphery might be clearer. Inadequate mydriasis made it impossible to examine more than the central area.

Not directly connected with this case, but worthy of note, is the observation that the mother presumably transmitted the disease to Mrs. N. W., a neighbor, who was then three and one-half months pregnant. Mrs. N. W.'s baby was stillborn as the result of an obstetric accident. The eyes were not examined. Autopsy disclosed a normal heart.

CASE 6 (J. W. T.).—The mother, aged 30, had a rash, presumably German measles, two weeks after her last menstrual period. This rash involved her face, with a few scattered lesions over the body. She did not feel well but did not go to bed. She does not remember many details of the illness and considered it trivial at the time. A daughter and several children living in the same block in Denver had German measles at the same time. The mother has one child in good health and has had one stillborn child. The mother's father and one brother have mild hypospadias. There was no other family history of congenital defects.

The baby, a boy, was born at term on Nov. 1, 1943, weighing 5 pounds 2 ounces (2,324.66 Gm.). The infant has presented a persistent feeding problem. At the age of 15 months he weighed 13 pounds 9 ounces (6,151.84 Gm.). There was a congenital heart defect producing a murmur heard throughout the cycle. The lesion was thought to be a patent ductus arteriosus. The infant was tongue-tied, and hypospadias of the penile portion was present. We first examined the boy on Feb. 11, 1945. He was seemingly alert and made an effort to look at objects. There was an inconstant and variable convergent strabismus. The eyes made coarse nystagmoid movements. Both eyeballs, including the corneas, were definitely smaller than normal. The pupils were equal and reacted moderately to light. Both lenses were quite opaque in the pupillary zones and no fundus reflex could be obtained. A mydriatic was not used.

COMMENT

In all 6 of the cases described rubella had developed in the mothers during the first two to six weeks of pregnancy. Three of the mothers did not know that they were pregnant when the exanthem appeared. The disease was mild and usually regarded as trivial. Few of the mothers remembered many of the details of the illness. In all of the cases there was a history of contact with some one suffering from rubella and in several cases there were multiple infections in the family. Five of the infections were acquired in Colorado and one in St. Louis. The earliest case was in 1942.

All of the babies had congenital cataracts. In 3 cases the cataracts were bilateral and the lenses more or less completely opaque. One of the cataracts (case 3) apparently was membranous. There were 3 bilateral and 3 unilateral cases of microphthalmos. The corneas were measured in only 1 baby, but the defect was grossly apparent in all. The unilateral cataracts were primarily nuclear with a less opaque periphery. These nuclear cataracts conformed closely with the description given by Gregg.[1] Each of these 3 patients showed in the noncataractous eye diffuse pigment alteration in the fundus suggestive of changes resulting from chorioretinitis. Swan and associates [2] described "multiple small pigmented spots on the fundus" in 1 case. Vitreous opacities were found associated with the changes in the fundus in case 1. Sluggish pupillary reactions have been noted by most observers. In 2 of our cases it was our impression that the pupils reacted sluggishly shortly after birth but that the reaction was normal when the eyes were examined approximately one year later. In 2 of the infants the pupils failed to dilate well with several different mydriatics. One of the patients (case 2) had a hazy cornea that later cleared. Bilateral congenital dacryostenosis was present in case 5. It would seem that all of the intraocular findings can be explained on the basis of an intrauterine inflammatory reaction involving particularly the uveal tract.

Some type of cardiac lesion was present in all 6 of the babies, a septal defect being suspected in 4. The infants were somewhat smaller than average. Most had some difficulty in feeding. Microcephalus was not observed, but no measurements of the head were made. There was no attempt to evaluate the mental condition. There was 1 case each of talipes valgus and of cryptorchism. The patient with hypospadias had a strong family history of this condition, so we probably cannot ascribe this defect to the maternal rubella.

As rubella is a common disease, and as it doubtless in the past has infected a great many pregnant women, one may ask why this relationship to defects in the offspring had not been noted prior to 1941. This omission is particularly striking when one considers that common defects include a distinctive type of cataract and microphthalmos. It would seem probable that some new factor has developed to produce the congenital defects. Gregg [1] has expressed some doubt as to the disease being rubella. Swan and associates [2] studied this question carefully and concluded that the infection is rubella but that

the disease may have undergone some alteration in character. They [2b] later pointed out other evidence indicating some change in the disease. One may conjecture that the virus of rubella underwent some transformation in Australia and that this new strain was introduced into the United States. The introduction would not have been difficult with the current voluminous and rapid traffic between these countries.

In view of the serious malformations encountered every effort should be made to protect women in early pregnancy from rubella. Erickson [6] recommended the deliberate exposure of girls to rubella to immunize them before the child-bearing age. He further suggested the use, particularly during epidemics, of convalescent serum for all women who are in early pregnancy and have not had rubella. Strong [7] suggested that gamma globulin may prove of value in modifying the immunity to the disease. Therapeutic abortion has been recommended if rubella should occur during the first third of pregnancy. The gravity of the congenital lesions and the likelihood of their development would possibly seem to warrant this procedure.

7. Strong, R. A.: Rubella and Congenital Malformations, editorial, Internat. M. Digest **46**:60-62 (Jan.) 1945.

CONCLUSIONS

Congenital defects have been observed in six infants whose mothers had contracted rubella when from two to six weeks pregnant. Three of the babies had bilateral cataracts which were associated with bilateral microphthalmos. Three of them had unilateral microphthalmos with a distinctive type of cataract in the smaller eye. Lesions were observed in the fundus in the three eyes of this series in which the fundus could be seen. All 6 children had cardiac defects. There was 1 case each of talipes valgus, cryptorchism, hypospadias and dacryostenosis. We believe that the cataracts, the microphthalmos, the lesions of the fundus and the cardiac defects are the result of intrauterine damage by rubella.

EVALUATION OF TOXOPLASMA NEUTRALIZATION TESTS IN CASES OF CHORIORETINITIS

JOSEPH M. HEIDELMAN, M.D.
CINCINNATI

The purpose of this paper is to report the results of a study of the possible diagnostic significance of Toxoplasma-neutralizing antibodies in determining the cause of chorioretinitis.

REVIEW OF LITERATURE

Epidemiology.—Toxoplasma is a protozoón of uncertain classification first observed in the North African rodent gondi and named by Nicolle and Manceau [1] in 1909. Since then a large number of animal species, including birds, from various parts of the world have been described as natural hosts for this parasite. Animal toxoplasmosis is

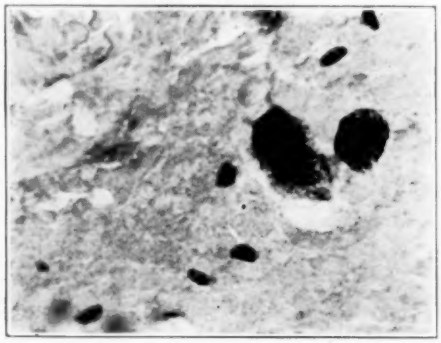

Fig. 1.—Toxoplasmas in a smear from the brain of a mouse. Wright's stain; × 950.

considered the source of human infection, although the manner of transmission among animals and from animals to man is unknown. The biologic and immunologic relationship between a human and an animal strain of Toxoplasma has been demonstrated.[2]

Properties of Toxoplasma.—In strained smears (fig. 1) the organisms are crescentic, oval or piriform in shape, measuring 4 to 7 microns in length and 2 to 4 microns in width. They consist of a distinct cytoplasm and a nuclear chromatin mass. With Wright's stain the nuclear chromatin is deep purple and the cytoplasm pale blue. In fixed tissues toxoplasmas are smaller and more rounded and often bear little resemblance to those observed in smears. They often occur in clusters or aggregates, commonly referred to as cysts

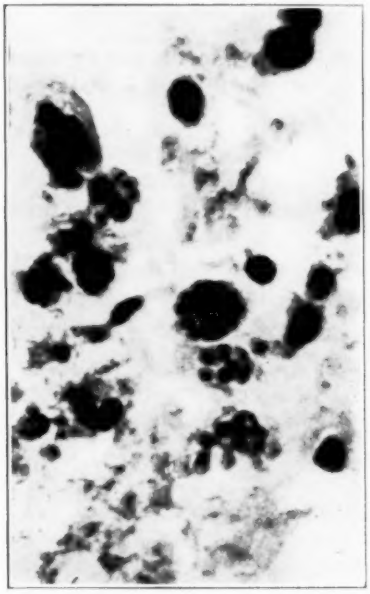

Fig. 2.—Toxoplasmic chorioretinitis, with parasitic "cyst" in the retinal lesion. Phloxine-hematoxylin stain; × 1,050. (from Koch, Wolf, Cowen and Paige [18]).

or pseudocysts (fig. 2). The parasites are nonmotile, and multiplication, which requires living tissues,[3] is by binary fission in the longitudinal plane.

Toxoplasmosis in Man.—The occurrence of human toxoplasmosis was first proved in 1939, when Wolf, Cowen and Paige [4] demonstrated

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University.

1. Nicolle, C., and Manceau, L.: Sur un protozaire nouveau du gondi Toxoplasma n. gen., Arch. Inst. Pasteur de Tunis **2**:97-103, 1909.

2. Wolf, A.; Cowen, D., and Paige, B. H.: Human Toxoplasmosis: Occurrence in Infants as an Encephalomyelitis; Verification by Transmission to Animals, Science **89**:226-227 (March 10) 1939. Sabin, A. B.: Biological and Immunological Identity of Toxoplasma of Animal and Human Origin, Proc. Soc. Exper. Biol. & Med. **41**:75-80 (May) 1939.

3. Sabin, A. B., and Olitsky, P. K.: Toxoplasma and Obligata Intracellular Parasitism, Science **85**:336-338 (April 2) 1937.

4. Wolf, A.; Cowen, D., and Paige, B. H.: Toxoplasmic Encephalomyelitis: III. A New Case of Granulomatous Encephalomyelitis Due to a Protozoan, Am. J. Path. **15**:657-694 (Nov.) 1939.

toxoplasmas at autopsy in the tissues of the central nervous system and the eye of an infant with encephalomyelitis and transmitted the infection to animals. There are at present 13 fatal cases of infantile toxoplasmosis on record. Nine of these cases, 4 of which were obtained from the literature [5] and had not previously been recorded as instances of the disease, were identified by Wolf and his associates.[6] One of the cases of the same authors had previously been reported by them as an instance of encephalitozoic encephalomyelitis.[6a] Of the remaining 4 cases, 2 were identified by Steiner and Kaump [7] and 2 by Zuelzer.[8] The diagnosis in 1 of the cases mentioned in the report of Steiner and Kaump was made by a restudy of the sections of the brain from a case referred to them by Sailer. The case reported by Hertig,[9] of an infant who died presumably of bacterial infection and in whose tissues protozoa were found which were classified as Sarcocystis by the author but later were recognized as toxoplasmas by Pinkerton and Weinman,[10] is not included as an example of the same disease.

Clinical Picture.—Fatal cases of toxoplasmic encephalomyelitis, as noted by Wolf and his co-workers, were characterized chiefly by convulsions, internal hydrocephalus, cerebral calcification and other neurologic symptoms or signs, and chorioretinitis. The spinal fluid was commonly xanthochromic, with increased protein and mononuclear pleocytosis.

Pathologic Features.—The pathologic changes in the central nervous system, according to the same authors,[11] consisted of areas of inflammation and necrosis and miliary granulomas, hydrocephalus and calcification. In some cases lesions were found in other organs, and in 1 case there was predominantly visceral involvement.[6b]

Similar areas of inflammation and necrosis were found in the retina (fig. 3). In the central portions of the necrotic areas all the layers of the retina were involved with perivascular and diffuse infiltration of lymphocytes, plasma cells and occasional neutrophils, eosinophils and lipid-laden phagocytes. There was endothelial hyperplasia of the capillaries, and an increase in glial tissue was sometimes seen, with extension into the vitreous. Disruption of the lamina including the pigment layer occurred in the more affected zones, with migration of pigment into the inner retinal layers. In areas corresponding to the retinal lesions the choroid was infiltrated with cells similar to those in the retina, and the sheaths of the optic nerve were similarly infiltrated. The sclera was normal. Toxoplasmas were present in the chorioretinal lesions (fig. 2).

Prenatal Inception of Disease.—In 1 of the cases of Wolf, Cowen and Paige [12] intrauterine hydrocephalus required craniotomy for delivery; in other cases the presence of symptoms during the first days of life or the pathologic age of the lesions suggested onset of infection before birth. Since all the mothers appeared healthy, the implication was that they harbored a latent infection. The possibility of the existence of an acquired type of infantile toxoplasmosis was mentioned by Sabin [13] and by Cowen, Wolf and Paige [14] and was recently considered by Zuelzer [8] in 1 of his cases.

5. Jankû, J.: Pathogenesis and Pathologic Anatomy of Coloboma of the Macula Lutea in an Eye of Normal Dimensions, and in a Microphthalmic Eye, with Parasites in the Retina, Časop. lék. česk. **62**:1021-1027, 1054-1059, 1081-1085, 1111-1115 and 1138-1143, 1923. Margarinos Torres, C.: Sur une nouvelle maladie de l'homme, caracterisée par la présence d'un parasite intracellulaire, très proche du Toxoplasma et de l'Encéphalitozoon, dans le tissu musculaire cardiaque, le muscles du squelette, le tissu cellulaire sous-cutané et le tissu nerveux, Compt. rend. Soc. de biol. **97**:1778-1781, 1927. Richter, R.: Meningoencephalomyelitis Neonatorum: Anatomic Report of a Case, Arch. Neurol. & Psychiat. **36**:1085-1100 (Nov.) 1936. de Lange, C.: Klinische und pathologisch-anatomische Mitteilungen über Hydrocephalus chronicus congenitus und acquisitus, Ztschr. f. d. ges. Neurol. u. Psychiat. **120**: 433-500, 1929.

6. (*a*) Wolf, A., and Cowen, D.: Granulomatous Encephalomyelitis Due to an Encephalitozoon (Encephalitozoic Encephalomyelitis), Bull. Neurol. Inst. New York **6**:306-371 (July) 1937. (*b*) Paige, B. H.; Cowen, D., and Wolf, A.: Toxoplasmic Encephalomyelitis: V. Further Observations of Infantile Toxoplasmosis; Intra-Uterine Inception of the Disease; Visceral Manifestations, Am. J. Dis. Child. **63**:474-514 (March) 1942. (*c*) Wolf, A., and Cowen, D.: Toxoplasmic Encephalomyelitis, in Blumer, G.: Practitioners Library of Medicine and Surgery, New York, D. Appleton-Century Company, Inc., 1940. (*d*) Wolf, Cowen and Paige.[4]

7. Steiner, G., and Kaump, D. H.: Infantile Toxoplasmic Encephalitis: Report of a Case, J. Neuropath. & Exper. Neurol. **3**:36-48 (Jan.) 1944.

8. Zuelzer, W. W.: Infantile Toxoplasmosis, with a Report of Three New Cases, Including Two in Which the Patients Were Identical Twins, Arch. Path. **38**:1-19 (July) 1944.

9. Hertig, A. T.: Sarcosporidia in the Myocardium of a Premature Infant: Report of a Case, Am. J. Path. **10**:413-418 (May) 1934.

10. Pinkerton, H., and Weinman, D.: Toxoplasma Infection in Men, Arch. Path. **30**:374-392 (July) 1940.

11. Wolf, Cowen and Paige.[4] Wolf and Cowen.[6a] Paige, Cowen and Wolf.[6b]

12. Wolf, A.; Cowen, D., and Paige, B. H.: Fetal Encephalomyelitis: Prenatal Inception of Infantile Toxoplasmosis, Science **93**:548-549 (June 6) 1941.

13. Sabin, A. B.: Toxoplasmosis, in De Sanctis, A. G.: Advances in Pediatrics, New York, Interscience Publishers, Inc., 1942.

(Footnotes continued on next page)

Other Forms of Toxoplasmosis.—Acquired toxoplasmosis was encountered in 2 children in the form of an atypical encephalitis by Sabin,[15] with survival in 1 case, and in 3 adults as an acute fatal exanthematous disease with pulmonary involvement, 1 case being reported by Pinkerton and Weinman[10] and the other 2 by Pinkerton and Henderson.[16] In all cases toxoplasmas were identified in the tissues, the spinal fluid or the blood. Among the apparent clinical and pathologic differences between the congenital and the acquired disease, of interest here, is the complete absence of ocular involvement in the latter.

Serologic Findings.—In 1937 Sabin and Olitsky[3] reported that Toxoplasma-neutralizing antibodies appeared in the serum of experimentally infected rhesus monkeys. The presence of this antibody in human serum was reported for the first time by Sabin[13] in a fatal case of toxoplasmic encephalitis verified at autopsy. Using the serologic method of these investigators, Wolf, Cowen and Paige[12] demonstrated Toxoplasma antibodies in the serum of mothers of infected infants and thereby furnished additional support for the early suspicion that the mothers in these instances were themselves infected.

Recognition of Congenital Toxoplasmosis During Life.—In 1941 Wolf, Cowen and Paige[12] mentioned the cases of 2 children in which the clinical diagnosis of toxoplasmic encephalomyelitis was made. These, with 4 other cases of infants or children who had a similar clinical picture, were described in a later report.[14] In most cases there was a history of onset of symptoms or signs early in life. Chorioretinitis, cerebral calcification and mental deficiency or psychomotor retardation were commonly associated features. Toxoplasmas were isolated by inoculation of mice with the ventricular fluid of a patient 2 months of age who had chorioretinitis, hydrocephalus and cerebral calcification. There was psychomotor retardation at the age of 7½ months. Forms resembling Toxoplasma were observed in a direct smear of ventricular fluid from another patient at 3½ months of age with the symptoms and signs just mentioned, and with epileptic seizures, which commenced in the fifth month of life. The serums of all 6 patients, whose ages ranged from 8 months to 11 years at the time the tests were made, had Toxoplasma-neutralizing antibodies, but this was true of only 2 of the mothers. The authors pointed out that the infection in the later phase may become inactive or healed, with the clinical manifestations occurring mainly as residual effects from the earlier period, and that the abnormalities of infants surviving an attack of toxoplasmic encephalomyelitis may erroneously be classified as congenital malformation of the

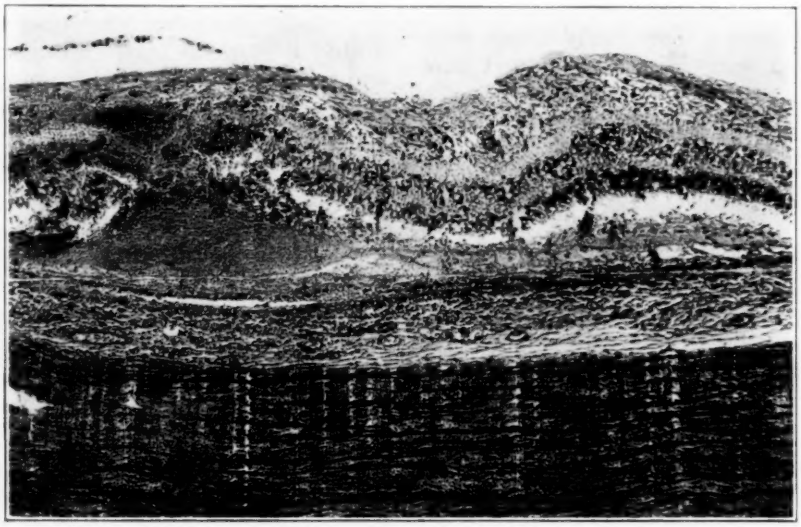

Fig. 3.—Toxoplasmic chorioretinitis, showing focal area of necrosis and inflammation in the retina and dense infiltration of the choroid. Phloxine-hematoxylin stain; × 125 (from Koch, Wolf, Cowen and Paige[18]).

14. Cowen, D.; Wolf, A.; and Paige, B. H.: Toxoplasmic Encephalomyelitis: VI. Clinical Diagnosis of Infantile or Congenital Toxoplasmosis; Survival Beyond Infancy, Arch. Neurol. & Psychiat. **48**:689-739 (Nov.) 1942.

15. Sabin, A. B.: Toxoplasmic Encephalitis in Children, J. A. M. A. **116**:801-807 (March 1) 1941.

16. Pinkerton, H., and Henderson, R. G.: Adult Toxoplasmosis: A Previously Unrecognized Disease Entity Simulating the Typhus-Spotted Fever Group, J. A. M. A. **116**:807-814 (March 1) 1941.

brain, congenital hydrocephalus, birth injury, epilepsy, etc.

In a publication which followed the preliminary report of Wolf and his associates, Sabin [13] described the case of an infant with chorioretinitis, cerebral calcification and hydrocephalus at 6 months of age. Ventricular fluid and biopsy specimens of the cortex were negative for Toxoplasma, but miliary granulomas were found in the tissue specimen. Psychomotor retardation was present at the age of 15 months. The diagnosis was corroborated by the same serologic method in the case of this patient and in the case of 8 other infants or children who had chorioretinitis or cerebral calcification or both associated with hydrocephalus or microcephaly or with convulsions and psychomotor retardation. The maternal serum was positive for Toxoplasma antibodies in every case.

Crothers [17] mentioned 10 cases in which the diagnosis of toxoplasmosis was supported by positive serologic reactions. There were 3 siblings in the group, 2 of whom had chorioretinitis, convulsions and cerebral calcification and the third the last condition only. Neutralizing antibodies were also found in the serum of normal members of the families of patients with clinical evidence of the disease, in addition to the mothers, whose serum regularly neutralized Toxoplasma.

Ocular Picture.—In the series of 15 cases of toxoplasmic encephalomyelitis reported by Wolf and his associates, including those identified from the literature, in which the diagnosis was made either clinically or at autopsy, chorioretinitis was present in 10 of the 11 cases in which ophthalmoscopic examination was made. In a stillborn infant the chorioretinal lesions were found at autopsy. Three patients had no clinical or histologic examination of the eyes. The chorioretinitis as described ophthalmoscopically [18] was invariably bilateral, and, with the exception of one eye, there was always macular involvement. Two patients, 31 days and 4 years of age, respectively, had lesions which showed slight activity; otherwise the chorioretinitis was healed. The acute or subacute lesions were characterized by edema, early necrosis and pigmentation. The healed lesions were sharply circumscribed, atrophic areas, varying in size, number, degree of proliferation and pigmentation. Squint, microphthalmos, nystagmus and optic nerve atrophy were commonly associated. Remnants of pupillary membrane, posterior cortical cataract and lenticonus were occasionally present.

The lesions in Sabin's cases were macular in position, although the number in which chorioretinitis existed was not stated and further descriptions were not given.

The chorioretinitis which was present in 7 of 10 cases reported by Crothers was not described.

Toxoplasma Antibodies Associated with Chorioretinitis or with Other Conditions.—Of 10 patients with chorioretinitis who were studied serologically by Sabin,[19] 9 had neutralizing antibodies. Four of these patients were children, 8 to 14 years of age, with visual disturbances noted earlier in life. Their mothers also had neutralizing antibodies. The other 6 patients, 5 of whom had antibodies, were adults 15 to 57 years of age at the time of onset of ocular symptoms. The lesions in 6 of Sabin's cases were described in a separate communication by Vail, Strong and Stephenson.[20] In general the lesions were similar to those in the cases of toxoplasmic chorioretinitis previously described. These authors suggested that a positive serologic reaction could be considered final evidence of a toxoplasmic origin in acquired as well as in congenital chorioretinitis.

Sabin [19] also found Toxoplasma antibodies in the serums of patients with unexplained encephalopathies or atypical pneumonia, of mothers who gave birth to anencephalic infants or infants with microcephaly or hydrocephalus and of normal persons,[21] including members of families of patients with clinical manifestations of toxoplasmosis.

MATERIAL FOR PRESENT STUDY

Serums.—Neutralization tests were performed on the serums of 211 persons one or more times for a total of 269 tests. These serums were obtained from patients with various forms of uveitis or other types of congenital or acquired ocular disease and from normal persons, including parents of patients with congenital chorioretinitis.

The serums were taken from patients in the wards and clinics of the Wilmer Ophthalmological Institute and the Harriet Lane Home for Children's Diseases of the Johns Hopkins Hospital, from patients at the Baltimore City Hospitals and from students at the

17. Crothers, B.: Toxoplasmic Encephalitis: Clinical Experience, Arch. Neurol. & Psychiat. **49**:315-319 (Feb.) 1943.

18. Koch, F. L. P.; Wolf, A.; Cowen, D., and Paige, B. H.: Toxoplasmic Encephalomyelitis: VII. Significance of Ocular Lesions in the Diagnosis of Infantile or Congenital Toxoplasmosis, Arch. Ophth. **29**:1-25 (Jan.) 1943.

19. Sabin, A. B.: Toxoplasma Neutralizing Antibody in Human Beings and Morbid Conditions Associated with It, Proc. Soc. Exper. Biol. & Med. **51**:6-10 (Oct.) 1942.

20. Vail, D.; Strong, J. C., Jr., and Stephenson, W. V.: Chorioretinitis Associated with Positive Serologic Tests for Toxoplasma in Older Children and Adults, Am. J. Ophth. **26**:133-140 (Feb.) 1943.

21. These persons were laboratory workers or rabbit handlers.

Maryland School for Blind Children. The normal serums were obtained from surgical, obstetric and newborn patients and from hospital employees.

Organisms.—Two strains of Toxoplasma were used in these tests. One originated from a fatal case of encephalitis and the other from a case of encephalomyelitis with a similar termination.[22]

TECHNIC

The method used for the determination of the presence or absence of neutralizing antibodies in serum was that described by Sabin and Olitsky[3] and by Sabin.[19]

TABLE 1.—*Criteria Used in Interpretation of Toxoplasma Neutralization Test*

Category of Unknown Serum	Relative Size of Cutaneous Lesions Yielded by Mixtures Containing Various Dilutions of Infected Mouse Brain Suspension			
	1:20	1:100	1:1,000	1:10,000
Negative	++++	++++	+++	++ or +
Negative	++++	++++	+++	—
Equivocal (repeat)	++++	+++	++ or +	—
Positive	++++ or +++	+++ or ++	—	—
Strong positive	++	—	—	—

1:500 and 1:5,000 are prepared with Tyrode's solution as the diluent. Equal amounts (0.15 cc.) of each serum to be tested (Tyrode's solution is used as the control) and 0.15 cc. of each dilution of the suspension of toxoplasmas are mixed in small tubes, resulting in final dilutions of 1:20, 1:100, 1:1,000 and 1:10,000 of all mixtures. After thirty minutes at room temperature, 0.2 cc. of each mixture is injected intradermally on the back of a shaved, clear-skinned rabbit into areas marked off with an indelible pencil.

During the early period of observation an injection wheal and the erythema reaction to serum appear but shortly subside. Toxoplasma lesions make their appearance after several days and increase in size until the seventh or eighth day. They are elevated indurated, pinkish lesions, and central necrosis and crusting occur in those resulting from the more concentrated mixtures. On the eighth day a record is made of the size of the papules and the area of necrosis by tracing on transparent paper. Tests with at least four serums and a control (twenty injections) can be accommodated on a single rabbit of ordinary size.

Interpretation of Results.—The serums are classified according to the degree of inhibition in the size of the test serum lesions and areas of necrosis as compared with the control lesions on the same rabbit. As indicated by Sabin, significant lesions are produced at the inoculated areas on almost all rabbits with the 1:20, 1:100 and 1:1,000 dilutions, but much less regularly with the 1:10,000 dilution, of the control mixtures. The last dilution was therefore omitted in 104 tests. Table 1, after Sabin,[19] contains the criteria used for interpretation of results in these tests.

TABLE 2.—*Incidence of Positive, Equivocal and Negative Results of Neutralization Tests on Various Types of Serum*

	Serums Tested	Number			Per Cent		
		Positive	Equivocal	Negative	Positive	Equivocal	Negative
Congenital chorioretinitis	27	11	6	9	41	22	37
Acquired chorioretinitis	59	5	3	51	8.5	5	86.5
Acquired anterior uveitis	38	1	3	34	2.5	8	89
Normal subjects							
(*a*) Mothers of patients with congenital chorioretinitis	7	5	1	1	70	14.5	14.5
(*b*) Fathers of patients with congenital chorioretinitis	2	0	1	1	0	50	50
(*c*) Others	58	4	2	52	7	3	90

Procedure.—Sterile precautions are observed in the collection of blood and the performance of the test. Because of the marked heat lability of the antibody, the serum is either tested on the day the blood is obtained or is frozen rapidly in sealed tubes and stored in a carbon dioxide refrigerator or preserved by means of lyophilization until used.[23]

Toxoplasmas are maintained for use by regular intracerebral passage of infected mouse brain suspension in the same species, death usually occurring between the fourth and the sixth day after inoculation.

At least two mouse brains are used in the test. These are removed when the animals are moribund and are weighed and ground in a mortar without an abrasive. A 10 per cent tissue suspension is made by the addition of Tyrode's solution.[24] This is allowed to precipitate spontaneously for thirty minutes in a refrigerator, after which the cloudy supernatant liquid is removed from the coarser particles. From the former, designated as the 1:10 dilution, dilutions of 1:50,

TABLE 3.—*Conditions with Which All Neutralization Tests Gave Negative Results*

	Number of Serums Tested
A. Congenital	
Macular degeneration	2
Optic nerve atrophy	3
Cataracts	2
Persistent tunica vasculosa lentis	1
Coloboma of iris	1
B. Congenital or acquired	
Retinitis pigmentosa	1
Retinal hemangioma	1
C. Acquired	
Keratitis	5
Inflammatory retinal detachment	2
Retinitis proliferans	1
Intraocular hemorrhage	1

RESULTS

The results of neutralization tests on all types of serums are given in tables 2 and 3.

22. These strains were furnished by Dr. A. Sabin and by Dr. A. Wolf respectively.

23. Negative tests which were obtained with serum kept at room temperature seventy-two hours or longer are not included in this series.

24. Isotonic solution of sodium chloride was substituted for Tyrode's solution in 198 tests because of the ready contamination of the latter.

The data in tables 2 and 3 lend themselves to comparison only in relation to the criteria used. For example, Cowen, Wolf and Paige [14] use six dilutions of the suspension of toxoplasmas between 1:20 and 1:1,600; this would enable the observer to note the point at which small differences between the test serum lesions and the control lesions occur. These investigators also use, in addition to buffered saline solution, normal serums as controls. The serums are classified as "positive" when the test serum lesions and the central areas of necrosis are in general one-half or less the size of the control lesions and are entirely inhibited in the higher dilutions of the suspension of toxoplasmas at which control lesions still appear, and as "suggestively positive" when the differences are distinct but less pronounced. When the contrast is minor or absent, the result is termed "doubtful" or "negative." The formulas used in Crother's series of tests were not given, although the results were designated as "strongly positive," "positive," "moderately positive," "doubtful" and "negative." In all probability there is general agreement among different observers as to the criteria for positive neutralization, the apparent differences being in the classification of serums in which the results are indecisive.

If equivocal results are considered to represent moderate neutralization, it can be stated that in 63 per cent of the cases of congenital chorioretinitis in which Toxoplasma might be suspected as an etiologic factor strong to moderate neutralization was obtained. It is interesting that the incidence of positive or equivocal results in patients with acquired chorioretinitis or anterior uveitis and in normal persons, exclusive of parents of infants or children with congenital chorioretinitis, was in the range of 10 per cent, which may represent the margin of error. While the per cent of parents, especially mothers, with antibodies was high, the number tested was too small to have a statistical value. The incidence of positive and equivocal results in the series

TABLE 4.—*Data in Cases of Congenital Chorioretinitis* *

Case No.	Patient	Age	Color	Sex	Microphthalmos	Nystagmus	Squint	Relative Size of Lesions Yielded by Serum-Toxoplasma Mixtures 1:20	1:100	1:1,000	1:10,000	Classification
1	R. S.	6 mo.	W	F	—	+	+	++	++	—	—	Positive
2	R. B.	7 yr.	W	M	+	+	+	+++	++	—	..	Positive
3	N. T.	11 mo.	W	F	—	+	+	+++	++	—	—	Positive
4	L. H.	1 mo.	N	M	+	?	?	+++	++	—	—	Positive
5	B. H.†	1 mo.	N	M	?	?	?	++++	++++	+	—	Negative
6	M. R.	17 mo.	W	M	—	+	+	++++	++++	++	+	Negative
7	D. M.	21 mo.	W	M	—	+	+	++++	++++	+++	+	Negative
8	B. J.	9 mo.	W	F	—	+	+	+++	++	—	..	Positive
9	A. B.	7 yr.	W	F	—	+	+	++++	+++	++	—	Equivocal
10	C. S.	9 mo.	W	F	+	+	+	++++	++++	+++	..	Negative
11	L. H.	7 yr.	W	F	+	+	+	++	++	—	—	Positive
12	J. C.	20 yr.	W	M	—	+	+	++++	+++	+	..	Equivocal
13	J. B.	21 yr.	W	F	—	—	+	++++	+++	+	..	Equivocal
14	W. M.	21 yr.	W	M	—	+	+	++++	++++	+++	++	Negative
15	T. W.	16 yr.	W	F	—	+	+	++	—	—	—	Strong positive
16	A. S.	15 yr.	W	M	+	+	+	++++	++	—	—	Positive
17	L. S.	22 yr.	W	F	—	+	+	++	++	—	..	Positive
18	E. S.	16 yr.	W	M	—	+	+	++++	++++	++	—	Negative
19	M. H.	14 yr.	N	F	—	+	+	++++	+++	++	—	Equivocal
20	J. M.	15 yr.	N	M	—	+	+	++++	+++	++	—	Equivocal
21	J. O.	13 yr.	W	M	—	+	+	++++	++	—	—	Positive
22	B. M.	14 yr.	W	F	+	+	+	++++	++++	++	—	Negative
23	T. H.	16 yr.	N	F	—	+	+	++++	++++	+++	+	Negative
24	A. B.	23 yr.	W	F	—	+	+	++++	++++	+++	..	Negative
25	G. S.	16 yr.	W	F	—	+	+	++++	++++	++	+	Negative
26	R. M.	25 yr.	W	M	—	+	+	++++	+++	+	..	Equivocal
27	S. J.	8 yr.	W	M	—	+	+	+++	++	—	—	Positive

* In this table, and in tables 5, 8 and 9, + indicates that the sign was present or that the reaction was positive; —, that the sign was absent or that the reaction was negative; ?, that information was not available and .., that the control lesion was inadequate for comparison or that no injection was made.

† The initial "B" is meant to represent "baby," since the infant was not named.

TABLE 5.—*Results for Parents of Patients with Congenital Chorioretinitis*

Patient's No. in Table 4	Patient	Parent	Relative Size of Lesions Yielded by Serum-Toxoplasma Mixtures 1:20	1:100	1:1,000	1:10,000	Classification
1	R. S.	Mother	+++	++	—	—	Positive
1	R. S.	Father	++++	++++	+++	..	Negative
2	R. B.	Mother	+++	++	—	..	Positive
3	N. T.	Mother	+++	+	—	—	Positive
4	L. H.	Mother	++	—	—	—	Strong positive
5	B. H.	Mother	++	—	—	—	Strong positive
7	D. M.	Mother	++++	++++	+++	+	Negative
7	D. M.	Father	++++	+++	++	—	Equivocal
8	B. J.	Mother	++++	+++	++	..	Equivocal
27	S. J.	Mother	+++	++	—	—	Positive

as a whole, 211 subjects, was 12 and 8 per cent respectively. The serums of 37 persons, or 22 per cent of those in the negative group, yielded a variable degree of neutralization in the 1 : 1,000 dilution of the Toxoplasma suspension, and in the 1 : 10,000 dilution when this was used. Sabin [19] obtained positive results with the serums of 39 per cent of 159 selected persons, but he did not state the number of equivocal results, if any, which were obtained.

macula was involved there was a temporal pallor of the disk. All lesions were inactive at the time of the test except those in one eye each in cases 12, 14 and 15.

Complete physical examinations and studies of the blood and the spinal fluid were performed on all infants. Serologic tests for syphilis were done in all cases and roentgenograms of the skull obtained in all cases except 9, 11 and 15. The patient in case 23 had congenital syphilis, and this was the probable cause of the chorioretinitis.

There were 5 cases of congenital chorioretinitis in which Toxoplasma antibodies were present and in which

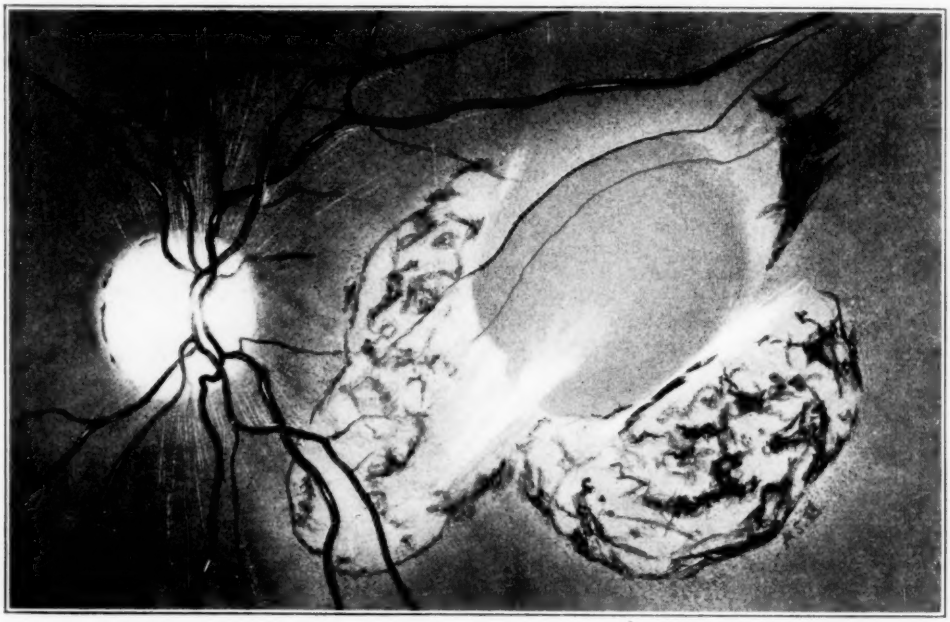

Fig. 4 (case 1, table 6).—Fundus of the left eye.

The data in all cases of congenital chorioretinitis are shown in table 4.

The data on all parents of patients with congenital chorioretinitis whose serum was tested are shown in table 5.

TABLE 6.—*Cases in Which Positive Signs of Toxoplasmosis Were Associated with Toxoplasma Antibodies*

Case No.	Patient	Age	Findings	Result of Test
1	R. S.	6 mo.	Cerebral calcification.....	Positive
2	R. B.	7 yr.	Cerebral calcification.....	Positive
3	N. T.	11 mo.	Convulsions; cerebral ventricular dilatation.....	Positive
4	M. H.	15 yr.	Cerebral calcification.....	Equivocal
5	L. H.	1 mo.	Cerebral calcification.....	Positive

Cases in Table 4.—The presence of chorioretinitis was established before the age of 2 years in the first 12 cases, while in the remaining 15 there was a history of ocular symptoms or signs from infancy. The chorioretinitis was unilateral in case 13; information on this point was uncertain in case 5 and the condition was bilateral in all of the rest. There was macular involvement in all eyes except those in case 10 and one eye each in cases 12 and 15. In all cases in which the

the diagnosis of toxoplasmosis was supported by other clinical manifestation, as shown in table 6.

Cases in Table 6.—CASE 1.—R. S. had had poor vision and crossed eyes from birth. There was a history of difficulty in feeding and a generalized cutaneous eruption in early infancy. Slight eosinophilia was found on the child's admission to the hospital at 6 months of age. These features have been described occasionally in cases of infantile toxoplasmosis.[14] The results of examination of the cerebrospinal fluid, including animal inoculations, were entirely negative for Toxoplasma. The patient was readmitted to the hospital at 16 months of age with convulsions and fever, which followed an attack of otitis media. Pneumococcus type XII was cultured from the cerebrospinal fluid, and the symptoms quickly subsided on combined penicillin and sulfadiazine therapy. The child is 24 months old at the time of this report and is slightly retarded mentally. Ophthalmoscopic examination showed that the media of the left eye were clear. In the macular region there was a large healed chorioretinal lesion, in the center of which was a blue-green, egg-shaped elevation of the retina, with fibrous attachments extending into the vitreous. The disk was yellow-white. The remainder of the fundus was normal. A picture of the left fundus is shown in figure 4. The fundus of the right eye was obscured by a heavy sheet of fibrous tissue, which extended to the back of the lens. There

was a macular lesion, similar to that found in the left eye. The cerebral calcification is shown in figure 5.

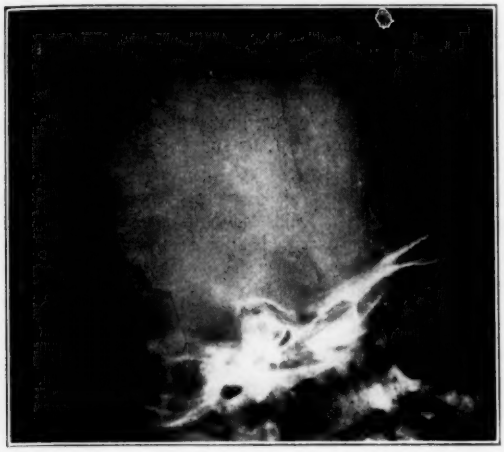

Fig. 5 (case 1, table 6).—Roentgenogram of the skull, showing areas of cerebral calcification.

congenital pyloric stenosis. Vomiting continued for several months. The convulsions, which were present at 11 months of age, consisted of spasmodic twitchings of the arms and legs associated with a sharp cry. At the time of the serologic test the spinal fluid was clear, colorless and under normal pressure, with 3 lymphocytes per cubic millimeter and 14.6 mg. of protein per hundred cubic centimeters. Organisms resembling those shown in figure 1 were seen with Wright's stain of the spinal fluid, but, unfortunately, the slide was broken before photographs could be obtained. Inoculation of this fluid into mice and guinea pigs was without results. The chorioretinitis was of the disseminated circumscribed type.

CASE 4.—An early history was not obtained in the case of M. H. In the left eye there was a chorioretinal lesion, similar to that shown in figure 6. An identical lesion had been described earlier in the right eye, but at the time of the examination the pupil on this side was occluded, as a result of later inflammation.

CASE 5.—L. H. exhibited uveokeratitis at 1 month and cerebral calcification at 2½ months of age. The eyes were microphthalmic, but the fundi were not seen until the infant was 5 months old, when bilateral macular chorioretinitis was found.

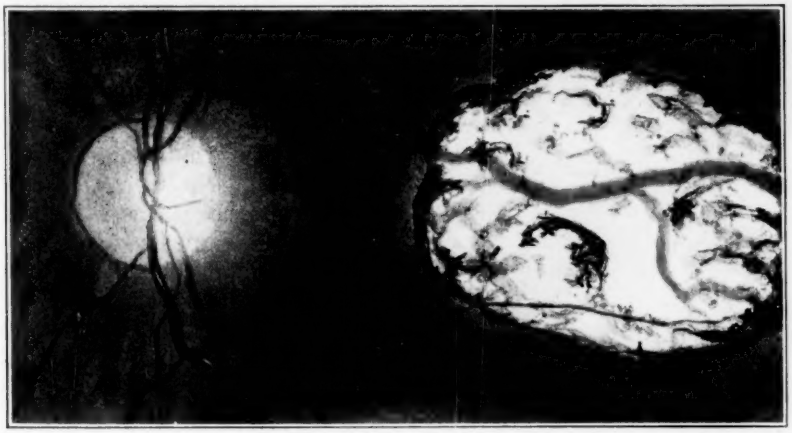

Fig. 6 (case 2, table 6).—Fundus of the left eye.

CASE 2.—R. B. had microphthalmos, healed bilateral macular lesions and cerebral calcification at the age of 2 years. When he was reexamined at 7 years of age, the right pupil was almost occluded by adhesions of the iris to a cataractous lens, and vision was reduced to the barest perception of light. Ophthalmoscopic examination of the left eye revealed a large, oval, inactive, sharply marginated chorioretinal lesion in the macula. The temporal portion of the disk was covered by a veil of glial tissue, which extended fanlike for a short distance and gradually blended with the normal retina on that side. The retinal arteries were moderately narrowed. Figure 6 shows the left fundus. The early description of the lesion in the right macula corresponded to that of the lesion in the left eye. Figure 7 shows the cerebral calcification. The cerebral condition shows no conspicuous change from that found at 2 years of age.

CASE 3.—N. T. had convulsions from the sixth day of life. Projectile vomiting commenced on the fourteenth day, at which time the patient underwent operation at another hospital on the basis of a diagnosis of

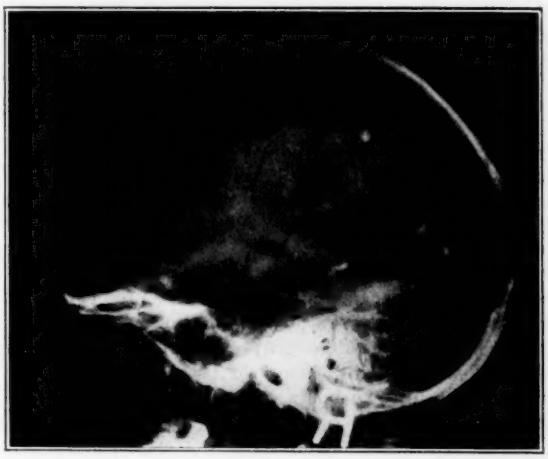

Fig. 7 (case 2, table 6).—Roentgenogram of the skull, showing multiple areas of cerebral calcification.

The diagnosis of toxoplasmosis was proved or was considered probable in 4 other cases in which there were congenital chorioretinitis and other evidence of the disease. The serologic tests gave negative results. These cases are included in table 7.

TABLE 7.—*Cases in Which Positive Signs of Toxoplasmosis Were Associated with Negative Results of Neutralization Tests*

Case No.	Patient	Age at Time of Test	Findings
1	B. H.	1 mo.	Parasitic cysts in tissues of central nervous system and eye at autopsy
2	D. M.	17 mo.	Hydrocephalus; psychomotor retardation
3	M. R.	21 mo.	Convulsions; dilatation of cerebral ventricles
4	E. S.	16 yr.	Hydrocephalus

Cases in Table 7.—The serums of B. H., case 1, table 7, and L. H., case 5, table 6, who were identical twins, and the serum of their mother were furnished by Dr.

Fig. 8 (case 4, table 7).—Roentgenogram of the skull, showing elongation in the anteroposterior diameter, irregular areas of rarefaction of the inner tables of the cranial bones and widening of the sella, associated with hydrocephalus.

W. W. Zuelzer,[8] who has described the clinical and pathologic aspects of these cases. The lesions in the eyes are to be the subject of a separate report by Zuelzer. Iridocyclitis and macular chorioretinitis with toxoplasmas in the lesions were found in the right eye of B. H. at autopsy. The serum was obtained twelve hours post mortem and dried from the frozen state twenty-four hours later. The result of the test on this serum was reported as "doubtful," since it neutralized the 1:1,000 and 1:10,000 dilutions of the suspension of toxoplasmas, but it is included in the negative group because it was inactive against the 1:100 dilution. It is possible that the delay in obtaining and preserving the serum may have been responsible for the weak neutralization in this case, although positive results have been obtained with serum which had been en route in the mail for seventy-two hours or more in the unpreserved state.

D. M., case 2, exhibited a maculopapular eruption and spasticity of the arms and legs from the sixth month of life. The results of studies of the blood and spinal fluid, including animal inoculations, were entirely negative for Toxoplasma.

The seizures of M. R., case 3, consisted of spasmodic contractions of the arms and legs and twitches of the face, which commenced at the age of 6 months. On the child's admission to the hospital, at 17 months of age, the white blood cell count was 16,300, with 60 per cent lymphocytes. The spinal fluid was normal.

E. S., case 4, had convulsions during the first year of infancy. Evidence of long-standing hydrocephalus is shown in figure 8.

The last 3 patients were greatly retarded in mental development. D. M. and M. R. (cases 2 and 3) had disseminated circumscribed chorioretinal lesions, while the lesions in the eyes of E. S. (case 4) were identical with the condition shown in figure 6.

Seven cases of congenital chorioretinitis included in tables 4, 6 and 7 were from the Maryland School for Blind Children. The serum was positive for Toxoplasma in 1 case, equivocal in 2 cases and negative in 4 cases. One patient, M. H., table 6, whose serum yielded an equivocal result had cerebral calcification, while another, E. S., table 7, whose serum gave a negative reaction, had hydrocephalus (fig. 8). It is probable, therefore, that Toxoplasma is an etiologic factor of some importance in the blindness due to congenital chorioretinitis found in institutions of this kind.

Neutralizing antibodies have not been consistently demonstrated by other investigators in all patients with proved or probable toxoplasmosis or in patients suspected of having the disease. Sabin [15] obtained a negative result with the serum of a boy with encephalitis from whose spinal fluid toxoplasmas were isolated by inoculation of guinea pigs. The serum of a 14 month old infant with convulsions, microcephaly, chorioretinitis, cerebral calcification and psychomotor disturbance, described by Levin and Moore,[25] and that of his mother were also found negative for neutralizing antibodies [26] by Sabin.[13] In 2 other patients in the series of the same author [19] with some of the clinical manifestations of toxoplasmosis, including cerebral calcification or chorioretinitis, antibodies were not found in the serum. There were also 9 of 10 infants or children with histories of convulsions beginning soon after birth, psychomotor retardation or palsies not associated with cerebral calcification or chorioretinitis who were without antibodies. In another of Sabin's [13] patients, already mentioned, who presented chorioretinitis, hydrocephalus, cerebral calcification and psychomotor retardation, the serum showed only slight evidence

25. Levin, P. M., and Moore, H.: Fetal Toxoplasmic Encephalitis: A Type of Congenital Cerebral Disease, J. Pediat. **21**:673-679 (Nov.) 1942.

26. Complement-fixing antibodies were demonstrated.

of neutralization at the age of 6 months, but there was an increase in neutralizing antibodies in subsequent months.

The data in the 12 cases of acquired anterior or posterior uveitis in which positive or equivocal results were obtained are given in table 8.

Cases in Table 8.—The ocular lesions in all patients were in the active stage at the time of the test, although some of the patients had a history or clinical evidence of previous inflammation in the same or in the other eye. Some of the patients in the group were hypersensitive to tuberculin; others had blood agglutinins for Brucella or the complement fixation test gave a positive reaction for gonococci; several had chronic tonsillitis or sinusitis, and 1 had syphilis.

TABLE 8.—*Cases of Acquired Uveitis Associated with Toxoplasma-Neutralizing Antibodies*

Patient	Color	Sex	Age, Yr.	Diagnosis	Relative Size of Lesions Yielded by Serum-Toxoplasma Mixtures 1:20	1:100	1:1,000	1:10,000	Classification
R. J.	W	F	35	Posterior uveitis	+++	++	—	—	Positive
N. S.	W	M	34	Posterior uveitis	++++	++	—	—	Positive
H. C.	W	M	30	Posterior uveitis	++++	++	—	—	Positive
E. M.	W	M	20	Posterior uveitis	+++	++	—	—	Positive
M. P.	W	F	20	Posterior uveitis	++++	++	—	—	Positive
J. J.	W	M	52	Posterior uveitis	++++	+++	++	..	Equivocal
J. P.	W	M	29	Anterior uveitis	+++	++	—	—	Positive
G. B.	N	M	35	Anterior uveitis	++++	+++	+	..	Equivocal
O. S.	W	M	30	Posterior uveitis	++++	+++	+	—	Equivocal
R. P.	W	F	36	Anterior uveitis	++++	+++	++	—	Equivocal
C. B.	W	M	57	Anterior uveitis	++++	+++	++	—	Equivocal
I. P.	W	F	35	Posterior uveitis	++++	+++	++	—	Equivocal

TABLE 9.—*Normal Persons Whose Serum Neutralized Toxoplasma*

Patient	Race	Sex	Age	Relative Size of Lesions Yielded by Serum-Toxoplasma Mixtures 1:20	1:100	1:1,000	1:10,000	Classification
E. J.	N	F	17	+++	++	—	—	Positive
C. K.	N	F	21	++++	++	—	—	Positive
G. T.	N	F	19	++++	++	—	—	Positive
C. W.	W	F	17	++++	+++	++	..	Equivocal
M. B.	N	F	18	++++	+++	++	—	Equivocal
L. M.	N	F	29	++++	++	—	—	Positive

Particular mention should be made of R. J., who is also included among the parents in table 5 and who is the mother of patient 27 in table 4; her serum also yielded a positive reaction. She had a unilateral, round, nonpigmented, grayish white, slightly elevated macular lesion, 1 disk diameter in size. On one occasion posterior corneal precipitates and an aqueous flare were noted in the same eye. Except for pronounced sensitivity of the skin to tuberculin, a complete clinical survey revealed nothing abnormal.

The data for the normal subjects, other than parents of patients with congenital chorioretinitis, whose serums gave a positive or an equivocal reaction for Toxolplasma are shown in table 9.

The reason for the positive results in these cases is not clear. It is notable, however, that 5 of the 6 persons tested were Negro women in the maternity ward, all being tested ten days post partum. One of these patients had preeclampsia, while 3 had had postpartum infections, with moderate to high temperatures. The infants in all cases were normal and remained so during an observation period of ten months. The serums of 3 patients which were tested had no antibodies. Also, the previous offspring of all the women had been normal. There were 6 other obstetric patients, without postpartum infection, whose serums were negative. It seems unlikely that 5 patients taken at random from a single ward would have latent toxoplasmosis with specific antibodies whereas patients with definite clinical evidence of the disease were without them. The impression is, therefore, that the antibodies in at least some of these patients were nonspecific.

NONSPECIFIC SERUM REACTIONS

In the group of cases of congenital chorioretinitis in which there was definite reason to suspect Toxoplasma as the etiologic agent, the incidence of positive or equivocal reactions was 63 per cent. From these results it would appear that a positive reaction in congenital chorioretinitis has definite diagnostic value. In the other groups, such as those cases of acquired anterior or posterior uveitis, and in normal persons antibodies were present in 10 to 14 per cent. On the other hand, negative reactions were obtained in 4 cases in which the diagnosis of toxoplasmosis appeared certain. An attempt was therefore made to find an explanation for the paradox of positive reactions in normal persons and negative reactions in the presence of disease, and to determine the conditions under which nonspecific neutralization of Toxoplasma, as suggested by the foregoing data, might occur.

The method used was that indicated by the results of the investigations of Sabin and Ruchman.[27] These authors observed that the neutralizing antibody appeared in rhesus monkeys as early as two weeks after infection and per-

27. Sabin, A. B., and Ruchman, I.: Characteristics of the Toxoplasma Neutralizing Antibody, Proc. Soc. Exper. Biol. & Med. **51**:1-6 (Oct.) 1941.

sisted throughout the period of observation (fourteen months) without evidence of a persistent infection. The antibody was of low titer and was destroyed in serum exposed to a temperature of 56 C. for thirty minutes. The neutralizing antibody which was present in the serum of an infant with congenital toxoplasmosis was similarly found to be thermolabile and of apparently low titer. The authors further described the results in neutralization that they had obtained with "hyperimmune" monkey serum, which was prepared by pooling the serum of monkeys repeatedly inoculated with Toxoplasma-infected tissues. This serum, which had originally yielded the low titer neutralizing antibody, after interone to four weeks, unheated serum still gave either positive or equivocal reactions. However, tests performed with unheated and heated portions of serums which were obtained nine to

TABLE 10.—*Cases in Which the Serum Was Tested for Thermolability of the Antibody*

Patient	Age	Positive Findings	Reaction of Serum: Portion Unheated	Reaction of Serum: Portion Heated at 56 C.
R. S.	15 mo.	Congenital chorioretinitis, cerebral calcification	+	—
L. H.	1 mo.	Congenital uveokeratitis, cerebral calcification	+	—
R. B.	7 yr.	Congenital chorioretinitis, cerebral calcification	+	—
L. S.	23 yr.	Congenital chorioretinitis	+	—

TABLE 11.—*Cases in Which Original Unheated Serum Gave a Positive Reaction and Both Heated and Unheated Portions Gave Negative Reactions Several Months Later*

Patient	Age	Clinical Findings	Original Specimen II Unheated	Interval Between Venipunctures	Specimen III Unheated	Specimen III Heated, 56 C.
E. M.	20 yr.	Acquired posterior uveitis.....	+*	17 mo.	—	—
J. P.	29 yr.	Acquired anterior uveitis.....	+	21 mo.	—	—
G. T.	19 yr.	Normal.....	±	9 mo.	—	—
C. K.	21 yr.	Normal.....	±	9 mo.	—	—

* In this table, and in table 12, + indicates a positive reaction; ±, an equivocal result, and —, a negative reaction.

TABLE 12.—*Cases in Which Original Unheated Serum Gave an Equivocal Reaction and Both Heated and Unheated Portions Gave Negative Reactions Three Weeks and Ten Months Later*

Patient	Age	Clinical Findings	Original Specimen I Unheated	Interval Between Venipunctures	Specimen II Unheated	Specimen II Heated, 56 C.
J. C.	20 yr.	Congenital chorioretinitis.....	±	10 mo.	—	—
C. W.	18 yr.	Normal.....	±	3 wk.	—	—

vals of four and seven years' storage in an ordinary refrigerator was found to have a high titer antibody, which was not destroyed by heating the serum at 56 C. for one-half hour. They concluded that this thermostabile "hyperimmune" reaction was not due to the regular neutralizing antibody.

The following measures were carried out to determine, if possible, the specificity of the neutralizing antibody according to the method suggested by the aforementioned authors. A number of serums were divided into two portions, and one part was tested in its natural state and the other after being heated at 56 C. for thirty minutes. Table 10 shows the results in 4 cases, in all of which the unheated portion of serum gave positive results and the heated portion negative results, and confirms the observations of Sabin and Ruchman on the thermolability of the regular, low titer neutralizing antibody.

Table 11 shows the results in 4 cases in which the unheated serum had formerly yielded at least one positive reaction. When retested in from twenty-one months later gave negative results in all cases.

Table 12 shows 2 other cases in which equivocal results were obtained with the original unheated serum and in which negative results were obtained with both the unheated and the heated portion of the serum obtained three weeks and ten months later.

An analysis of the results of this small number of cases shows that in all cases the antibody was of low titer and probably the same. In the 6 cases shown in tables 11 and 12 the antibody disappeared spontaneously in a period of three weeks to twenty-one months. This, however, was not a uniform phenomenon, since in 3 cases of congenital chorioretinitis not shown in table form the antibody was still present nine to fifteen months after the original positive test. The fact that the results of the test can be reproduced with remarkable precision with preserved portions of the same specimen of serum whereas the differences are noted with serum which is obtained later suggests that the variable factor in neutralization is humoral in origin.

Since a variable antibody content of the serum was demonstrated in 4 persons, table 11, with elevated temperature, spontaneous in 2 patients with postpartum infections and induced by means of intravenous administration of typhoid vaccine in 2 others with acquired uveitis, fever as a possible cause of nonspecific antibody production is suggested. However, similar observations were made on 2 other persons, table 12, with normal temperatures, 1 of whom had chorioretinitis from the fourth month of life. In the patient last mentioned there was evidence of a reactivated chorioretinal lesion in one eye at the time of the original test. Summing up the results in the cases in tables 10, 11 and 12, it would appear, first, that the low titer neutralizing antibody is thermolabile and, second, that there is a tendency for it to disappear spontaneously from the blood serum. This observation would explain the negative results obtained in the 4 cases of congenital toxoplasmosis, although an alternative possibility, as suggested by Sabin,[13] is that the antibody may not be produced early in all instances. It is evident that in some cases the antibody may persist for many months, or even years. However, there is no definite explanation for what appear to be false positive reactions. In this series the high titer, thermostabile neutralizing antibody described by Sabin and Ruchman as occurring in "hyperimmune" monkey serum was not found in any human serums, although a potent neutralizing antibody which was not inactivated at a temperature of 56 C. for thirty minutes was found in the serum of immune rabbits. This study, therefore, does not support the implication which follows from the results of the investigations of these authors that the nonspecific antibody would be thermostabile. It does suggest, though, that nonspecific serum reactions might occur in 10 to 14 per cent of persons without clinical evidence of toxoplasmosis as it is at present understood.

Other possible factors which might cause a nonspecific serum response were investigated. It seemed possible that a variation in the p_H of the saline diluent for the suspension of toxoplasmas might be a responsible factor. Accordingly, 2 serums which had been positive ten and twenty-one months previously were retested, using diluents of varying p_H between 5.9 and 7.5. Unfortunately, all of these tests gave negative results, the antibody having spontaneously disappeared; so there is no information available on this point.

The possibility that the results might be influenced by the difference in the strains of Toxoplasma was considered. However, in many cases the variation in results occurred with the same strain, and there were 3 serums in the group which neutralized both strains of Toxoplasma. Moreover, monkey serum[28] which came from monkeys infected with one strain neutralized both strains of Toxoplasma. Therefore there is no evidence from this study that the strain of organisms used in the test would affect the results.

SUMMARY AND CONCLUSIONS

Strong to moderate neutralization of Toxoplasma was obtained with the serum of 63 per cent of 27 patients with congenital chorioretinitis, 14 per cent of 97 patients with anterior or posterior uveitis and 10 per cent of 58 normal persons other than the parents of infants or children with congenital chorioretinitis. Of 9 patients with congenital chorioretinitis and other evidence of toxoplasmosis only 5 had antibodies. Antibodies were present in 6 of 7 mothers of patients with congenital chorioretinitis. Therefore it would appear that the demonstration of the neutralizing antibody should be considered a factor of moderate diagnostic value only in patients with congenital chorioretinitis. Its absence from serum does not rule out the possibility of toxoplasmic infection.

The neutralizing antibody is of low titer, is thermolabile and shows a tendency to disappear from the blood serum in a few weeks, although it may persist for fifteen months or longer, possibly even indefinitely in some cases. Aside from possible instances of familial infection, Toxoplasma-neutralizing antibodies may be demonstrated in 10 to 14 per cent of persons without clinical manifestations of toxoplasmosis as the disease is at present understood. It is probable that at least in some of these persons the antibodies are nonspecific.

Dr. Edwards A. Park, director of the department of pediatrics of the Johns Hopkins Medical School, permitted the study of various patients in his services and offered laboratory facilities at the Harriet Lane Home; Dr. W. W. Zuelzer, of the Children's Hospital of Michigan, furnished the serums and the histories in his cases; Major A. B. Sabin, formerly of the Children's Hospital of Cincinnati, and Dr. A. Wolf, of Columbia University College of Physicians and Surgeons, furnished the strains of Toxoplasma used; Major A. B. Sabin gave a generous supply of Toxoplasma-immune monkey serum, and Miss Helen Zepp and Miss Elizabeth Fisher assisted in the details of the laboratory technic.

808 Union Central Building.

28. Serum supplied by Major A. B. Sabin.

Ophthalmologic Reviews

EDITED BY FRANCIS HEED ADLER

HERPES ZOSTER OPHTHALMICUS

REPORT OF CASES AND REVIEW OF LITERATURE

AMBROSE EARL EDGERTON, M.D.

SAN FRANCISCO

Herpes zoster ophthalmicus presents an interesting problem. Although the disease was known to physicians of antiquity, their ideas concerning the disorder were obscure. They described, in considerable detail, the characteristics of the disease, but their interpretations were brief. The disease was known as zoster to the Greeks, and Pliny, a Roman, is said to have been the first to apply to the eruption the denomination of zona. From these ancient times to the early nineteenth century the literature is scant on the subject. Mahlis, in 1818, suggested that the eruption of herpes zoster followed the distribution of nerves, and Parrot, in 1856, noted that the eruption, like pain, developed along the course of branches of nerves, most frequently superficial, and that it was here that the neuralgias ordinarily manifested themselves. This was proved in 1861 by von Bärensprung. Hutchinson, in 1866, and Bowman, in 1867, were the first to describe herpes zoster ophthalmicus in detail, and each reported several cases.

An enormous amount of work has been done in recent years in the investigation of the pathology, treatment and various manifestations of zoster and other herpetic diseases. Although the condition is comparatively rare, the literature on this subject is large, a great many cases having been reported.

Herpes zoster has been noted to occur in the proportion of 1 to 2 per cent of all diseases of the skin. Horner found 2 instances in 28,328 cases of cutaneous disease during a six year period. Joseph found 163 cases of herpes zoster in 15,603 cases of diseases of the skin; Knowles, 286 cases in 21,337 cases, and Greenough, 235 cases in 17,741 cases. Fouchard, in 1898, found 57 cases of ophthalmic zoster in 5,000 cases of diseases of the eye. Da Fonseca, in 1882, saw 4 cases of ophthalmic zoster in 13,000 cases of ophthalmic disease, and Galezowski encountered 19 cases among 36,000 cases of diseases of the eye. Head and Campbell found 18 cases of the ophthalmic form in 416 cases of herpes zoster. Berggreen and Schüler, in 1938, reported 2,014 cases of herpes zoster occurring in Berlin, in 16 of which the fifth nerve was involved. Schönfeld encountered disturbances of ocular innervation in 12 per cent of cases. Only 5 cases were seen at the Wills Hospital in 1913-1914, out of a total of 30,000 cases of ocular disease.

Laqueur, in 1870, had found 52 instances of ophthalmic zoster in the literature, and Armaignac, in 1884, observed that a total of 200 cases had been reported. There are several varieties, distinguished mainly by the region involved. In 1924 Achard stated that cases of the ophthalmic type represented about 7 per cent of the cases of all types of herpes zoster. Ophthalmic zoster is, after thoracic zoster, the most frequent type, and, like the diseases in other localizations, it is usually unilateral and nonrelapsing. At times its frequency amounts to an epidemic, as reported by Head and Campbell, Trousseau, and Levaditi, and at other times it is seldom seen. Various manifestations of the disease are continually being reported, but little is definitely known. Theories regarding its cause are frequently being advanced, but the etiologic factors are still obscure.

The disease may be of long duration, the period ranging from two weeks to several months, and occurs with greatest frequency and with most severity in the latter half of life. It displays no predilection for age, color or sex. It may be confined to certain branches of the fifth nerve, and it is observed most frequently on the inner half of the upper lid, the adjacent side of the nose, over the eyebrow and in the region of distribution of the supratrochlear, the infratrochlear, the supraorbital and the oculonasal nerve. The area most frequently affected is that of the supraorbital nerve, the lesions often exhibiting a symmetric design along various ascending and descending branches of this nerve, and next in frequency is the area of the supratrochlear nerve. The frontal nerve may be affected alone, and

A thesis presented to the American Ophthalmological Society, in partial fulfilment of the requirement for membership, March 1942.

some believe that this nerve is always involved. Rossander, in 1877, described a case, however, in which only the infratrochlear nerve was affected. The disease may be localized along the lacrimotemporal nerve and involve the temple. The more serious complications occur when the lacrimal and nasociliary branches are affected. The entire territory of the ophthalmic nerve may be involved: namely, the upper lid, which is swollen and covers the globe; the internal frontal region, on which are distributed the vertical rows of vesicles, arranged in the form of a fan, and the anterior third of the scalp and the foot of the nose. Sometimes a single branch is affected: for example, the frontal, causing involvement of a large triangular territory, with a superior base; or the nasal branch, resulting in involvement of the internal third of the upper lid and the ala nasi; or the lacrimal branch, with consequent implication of the external third of the eyelid. Bär, in 1925, reported a case, from which he drew interesting deductions. In addition to cutaneous anesthesia in the frontal region, the upper lid, the conjunctiva and the cornea, on the right side, there was involvement of the ophthalmic division of the fifth nerve with the exception of the terminal branches of the nasociliary and anterior ethmoidal nerves, resulting in diminution of sensation in the lower lid and the upper half of the side of the nose. From this derangement of sensibility, he concluded that twigs of the first division, as well as fibers from the second branch, of the fifth nerve supply the lower lid.

Herpes zoster ophthalmicus may be associated with zoster of the superior maxillary branch, with vesicles on the lower lid, the superior maxillary region as far as the upper lip and the malar bone, the tonsils and the velum palati; with zoster of the inferior maxillary branch, with vesicles on the chin and the lower lip; with geniculate zoster, with vesicles in the external auditory canal and frequently with facial paralysis, and with zoster of the glossopharyngeal nerve.

Sometimes all nerves of the first division, or several of these branches, are affected simultaneously with the second division. Involvement of all nerves of the first and second divisions of the nerve is less often seen, and involvement of all three divisions together is rare. Cases of zoster without eruption are exceptional, although Lederer, in 1900, reported such cases.

ANATOMIC RELATIONS OF THE FIFTH NERVE

The physiologic makeup of the fifth nerve is complicated. The trigeminal nerve resembles a spinal nerve, being made up of a compressed group of afferent, posterior roots. Its ganglion, the gasserian, is a fusion of posterior root ganglions of all the posterior sensory roots, corresponding to all motor nerves from the brain stem. The nerve enters the pons midway between its lower and its upper border and sends an ascending root upward to the brain stem and a descending root to the tissues as far down as the second cervical level. Any pathologic process affecting the cells in the pons, such as meningitis, pontile tumor or inflammation, may be referred to the corresponding point of the peripheral distribution. In the main the nerve is sensory, with its center the gasserian ganglion, but it is linked up with fibers from the cervical portion of the sympathetic chain, which carry vasoconstrictor impulses and motor fibers to the levator palpebrae muscle, to Müller's muscle and to the fibers of the dilator pupillae.

The gasserian ganglion lies in the middle fossa of the skull, and from its upper portion arises the ophthalmic division of the fifth nerve, which passes into the cavernous sinus and runs along its lateral wall. The ophthalmic division gives off a branch to the tentorium, the recurrent nerve of Arnold, and sends filaments to the third and sixth nerves and sometimes to the fourth nerve. Involvement of this branch to the meninges may simulate symptoms of meningitis.

The ophthalmic division, the smallest of the three divisions of the fifth nerve, is a flat nerve, about 1 inch (2.5 cm.) in length, and is purely sensory. It is joined by sympathetic fibers from the superior cervical ganglion, and just before entering the sphenoid fissure, it divides into the frontal, the lacrimal and the nasociliary nerve.

The eye receives its sensory innervation from the ophthalmic division of the fifth nerve. Afferent impulses pass by this route to the gasserian ganglion and then to the pons. Some fibers end in the chief sensory nucleus, and others descend through the pons and the medulla to the upper segments of the spinal cord. These form the spinal root of the fifth nerve and form connections with the substantia gelatinosa of Rolando, which extends from the pons to the upper cervical portion of the cord. From the sensory nuclei, a second afferent neuron decussates to form the trigeminal fillet and then passes to the optic thalamus, where a third afferent neuron passes by way of the internal capsule and the corona radiata to the cortex. Thus, the fifth nerve fibers are exposed to injury over a wide area.

The first branch, the ophthalmic nerve, with the ciliary ganglion, supplies sensation to the upper lid, the conjunctiva, the eyeball, the lac-

rimal gland, the forehead, the anterior part of the scalp, the frontal sinus, the root and anterior portion of the nose and the caruncle; and a branch from the ciliary ganglion enters the optic nerve with the central artery of the retina.

The second branch, the superior maxillary nerve, with the sphenoid ganglion, furnishes sensation to the cheek, the anterior temporal region, the lower lid, the side of the nose, the upper lip, the upper teeth, the mucous membrane of the nose, the nasopharynx, the antrum, the ethmoid cells, the soft palate, the tonsils and the roof of the mouth.

The third branch, the inferior maxillary nerve, with the otic and submaxillary ganglions, is both motor and sensory and is distributed to the skin of the side of the head, part of the auricle and the external auditory meatus, the lower part of the face, the lower lip, the mucous membrane of the mouth, the tongue, the mastoid cells, the lower teeth, the gums, the salivary glands, the dura mater and the skull.

The frontal nerve is the longest branch of the ophthalmic nerve. It enters the orbit through the superior orbital fissure and divides into two branches, the supratrochlear and the supraorbital. The supratrochlear branch escapes from the orbit between the trochlea and the superior orbital foramen, passing up to the forehead, and gives off branches to the conjunctiva and the skin of the upper lid. The supraorbital branch passes through the supraorbital foramen, giving off branches to the upper lid, and ends in two cutaneous branches to the scalp. The supraorbital branch is the nerve most often affected with herpes zoster, and next in frequency is the supratrochlear; yet the latter rarely suffers alone. These nerves supply the upper lid and forehead and may extend as far back as the vertex.

The lacrimal nerve is the smallest branch of the ophthalmic division. It anastomoses with the facial nerve (pars intermedia of Wrisberg) and passes into the orbit through the superior orbital fissure, enters the lacrimal gland and gives branches to the gland, the conjunctiva and the skin of the upper lid. It is often difficult to tell whether or not this nerve is involved in cases of herpes zoster if the conjunctiva and the upper lid are affected, because they receive filaments also from the superior trochlear, from the frontal and from the inferior trochlear nerve. The temporal branch of the superior maxillary nerve in its course through the orbit receives a filament from the lacrimal nerve, and at times the zygoma may show vesicles, although the superior maxillary nerve itself may not be involved.

The nasociliary nerve becomes the main sensory nerve to the eyeball. This nerve crosses the optic nerve, and at the inner wall of the orbit it divides into two terminal branches, the infratrochlear nerve and the nasal nerve proper, supplying the iris, the ciliary body and the choroid. The infratrochlear nerve emerges from the orbit above the internal tarsal ligament. Its branches supply the sac, the conjunctiva, the skin of the lids and the root of the nose. As far as the eye is concerned, the nasal nerve is the most important. The nasal nerve proper leaves the orbit by the anterior ethmoid foramen to enter the anterior part of the cranium, at the inner margin of the cribriform plate. Here it turns forward under the dura and passes through a narrow opening at the side of the crista galli to reach the nasal cavity. It passes below the lower margin of the nasal bone and gives off branches to the skin and makes connections with the facial nerve. In its course, it sends a branch to the ophthalmic ganglion, a small fragment running alongside the optic nerve. It gives off the long root of the ciliary ganglion, from which short ciliary nerves pass to the iris; then it sends long ciliary branches to the ciliary muscle and the iris, and subsequently divides into the external and the internal nasal nerve, which supply the middle and the tip of the nose.

This nerve exhibits a complex distribution. Through its ciliary ramifications it furnishes sensibility to the globe; through its external course it innervates the internal part of the two eyelids, the lacrimal sac and the nose. Its internal distribution is partly to the nasal mucosa and partly to the skin of the lobe of the nose. The ciliary, or lenticulate, ganglion lies in the orbital fat between the optic nerve and the external muscles. It is made up of a filament from the nasal branch of the ophthalmic (sensory) nerve, fibers from the oculomotor nerve and a branch from the cavernous plexus of the sympathetic chain. Its branches are the short ciliary nerves, which accompany the long ciliary nerves and pierce the sclera near the entrance of the optic nerve. The short ciliary nerves are distributed to the cornea, the iris and the ciliary body. Inflammation of the ganglion may bring about dilation of the pupil, with increased ocular tension, through its sympathetic fibers.

The posterior parts of the sclera are supplied from the ciliary nerves. Anteriorly, the ciliary nerves form a plexus; fibers from this area are distributed to the anterior part of the sclera, behind the sclerocorneal junction (limbus), and go forward to the sclera. The corneal nerves enter this structure at about the middle third

of its thickness. These fibers form an anastomosis at the limbus, where about sixty branches enter the cornea.

Thus, the upper lid and the conjunctiva receive their sensory nerve supply from several branches of the fifth nerve—the supraorbital, the frontal, the infratrochlear and the supratrochlear. The lacrimal nerve supplies the lateral angle of the eye. The conjunctiva of the bulb likewise shares in the nerves of the lids and also gets some supply from the lacrimal nerve. Small branches of the ciliary nerve also enter the conjunctiva, where they combine with other nerves in the form of a plexus and then distribute themselves partly in the conjunctiva and partly in the sclera.

Königstein expressed the belief that the epithelium of the cornea is supplied by nerves arising from the conjunctival plexus; the substantia propria, by the superficial branches, and Descemet's membrane and the cornea over it, by the deep ramifications. His investigations also showed that the portion of the corneal nerves originating in the conjunctival nerves were developed in proportion to the development of the conjunctival portion of the cornea. When there is complete development of the pars conjunctivalis of the cornea, the epithelium of the cornea is supplied solely by conjunctival nerves. In that case the scleral portion of the cornea has its own, independent plexus.

Anomalous ramifications and an unconventional distribution of branches of the fifth nerve have been reported in some cases, and this should be taken into consideration in any problematic case of herpes zoster ophthalmicus. Arnold observed that the lacrimal nerve arose from two roots, one having its origin in the supraorbital nerve and the other in the nasociliary nerve in some cases. Svitzer saw a branch of the lacrimal nerve enter the bulb through the sclera and observed the radix longa of the ciliary ganglion arising from the supraorbital nerve. Pye, Howse, Davies and Colley noted the radix longa arising from the lacrimal nerve. Supernumerary roots of the ganglion have been described by Hyrti; one such root which he observed separated from the lacrimal nerve and entered the ciliary ganglion.

CLINICAL FEATURES

INCIDENCE

Age.—Apparently, in herpes zoster neither age nor sex assumes a decisive role, although it has been observed in children that pain is less severe, the course of the disease is shortened and symptoms of paralysis subside more readily. It is clear that observers are not agreed as to the time in life when the disease is most prevalent. In 2,250 cases of herpes zoster ophthalmicus the average age was 44. The disease may occur at any age but is more commonly seen among elderly people. They are more prone to attack when their physical condition is lowered, and many cases have been reported in which the zoster followed a recent illness or operation. Lodge and Lodge, in 1923, reported 20 cases, in which the average age was 55. Strzeminski stated that the disease developed ordinarily in middle life, rarely in youth or infancy. Rayer claimed that the disease was more frequent in adults. Brissaud found that most patients were between 60 and 70 years of age. Elliot found the average age to be 41, and Hewlett, 48.

On the other hand, Fox claimed that the disease was common in the young. Evans found that one half of his patients were under 14 years of age. Bateman stated that the condition occurred most frequently between the ages of 12 and 25 years. Fagge and Pye Smith found 100 cases, in 46 of which the patient was under 20 years of age. Crocker reported that three fourths of the patients seen were under 13 years of age. Stelwagon noted that the disease was most frequent in persons between the ages of 10 and 30 years. Head reported 378 cases, in 283 of which the patient was under 25, with an average age of 12 years. Rollet, Bujadoux and Blanc, in 1931, described a case of the disease in a girl of 10 years, with involvement of all three branches of the nerve on the right side and associated paralysis of the ocular muscles. Muscular paralysis as a complication is rare in children. Cases of ophthalmic zoster in children have been reported by Ginestous, Agnello, Fisher, Lederer, Desobry, McMurray, Gallemaarts, Rollet and Bussy, Halipré, Roll, Jessop, Koch, Knox, Mayou, MacNab, Knowles, Rachmaninow and others. Bonar and Pearsall saw a case of the disease in an infant 4 days old, and Lomer cited 2 cases of Bohn's in which the disease occurred in infants 5 and 7 months of age. Kolb, in 1909, described a case of a disorder in a newborn infant in which multiple groups of scars were symmetrically arranged in the area of the first and second divisions of the fifth nerve; these lesions he considered the remains of a bilateral herpes zoster ophthalmicus present in intrauterine life. There are apparently two periods in life in which herpes zoster is most likely to occur—under 14 and over 40 years of age.

Sex.—Some authors report a predominance of zoster in males; others claim that a greater number of females are attacked, and some believe that males and females have the disease

with equal frequency. Lodge and Lodge found the incidence to be the same in the two sexes. Evans found that females had the disease more often than males, the incidence being 75 per cent. Hewlett observed more cases of zoster in females. In the fifth and sixth volumes of the reports of the Royal London Ophthalmic Hospital are described 51 cases, 31 of males and 20 of females. Head (cited by Römer, in 1910) stated that in the London General Hospital in one year herpes zoster occurred in about 1 of 500 cases. Of 378 cases of all types of the disease, males were affected in 240 and females in 138. Hybord reported that males were more often affected than females, and this opinion was concurred in by Jaksch, Koch, Laqueur, Pacton, Aubineau, Strzeminski and Disson. Cantonnet, in 1935, claimed that the disease affected males in three fourths of the cases and the left side in two thirds of the cases. Davidson found that 75 per cent of patients were males; Joseph, 70 per cent; Brissaud, 75 per cent; Knowles, 70 per cent; Greenough, 45 per cent, and Metz, 65 per cent. I found that males were affected in 54 per cent of 2,250 cases of herpes zoster ophthalmicus. The right eye was affected in 54 per cent of all cases.

Seasonal Factors.—The seasonal occurrence varies. Many believe it to be associated with the cooler months of the year, but epidemics have occurred in the summer months as well. Neligan, in 1852, said that in the summer and autumn of some years the disease would appear to be epidemic among children. Parsons claimed that the disease had a definite seasonal incidence—in the spring and in the fall. Schamberg called attention to the predominance of cases in the spring and autumn. Brain claimed that the same seasonal incidence existed. Elliot, in 1918, reported 19 cases that occurred in India between September and March. Von Bókay, in Budapest, in 1928, reported more cases in December and January, about one month after the incidence of varicella had reached its peak. Knowles encountered the largest number of cases in July and August, while Stanford, Greenough, Blaschko, Joseph, Head and Campbell reported the occurrence of more cases in the spring. Head stated the belief that the disease was associated with an atmospheric influence. Recent investigators claim that the disease is most frequent during October and November.

EXPOSURE

Many investigators believe that herpes zoster develops as the result of chilling of the body, due to exposure to wind, cold and dampness. Paget, in 1866, reported a case in which the disease developed in a man aged 25 after exposure to severe cold. Three days after exposure an eruption appeared on the right side of the upper lip and nose and the right cheek, involving the first and second branches of the fifth nerve. Jeffries, in 1871, described 3 similar cases. Stieren reported 16 cases in 1906, in all of which there was a history of exposure to cold and dampness. He expressed the belief that the disease was due to climatic conditions and personal habits. Klinedinst, in 1918, cited 3 more cases in which the eruption followed exposure. Other cases in which there was a similar history have been described, among others, by Eyer, Hinde, R. F. Moore, Lagarde, DaFonseca, Hybord, Horstmann and Martini.

PRODROMAL SYMPTOMS

The general prodromal symptoms of malaise, headache, nausea, chills, fever and anorexia usually precede the eruption by several days. These symptoms are sometimes absent, the prodrome consisting merely of local pains and being characterized by unilateral neuralgia. The fever usually recedes at the time of the cutaneous eruption. Preliminary gastric disturbances are sometimes present and are due to existent relations between the trigeminal and the vagus nerve. The cutaneous temperature is increased on the affected side, with anesthesia of the surface of the skin. The flushing and redness of the skin is sufficient to raise the cutaneous temperature, as was first reported by Horner, in 1871, and by Paton, in 1926. The latter found that the temperature of the affected side was about 2 degrees (F.) higher than that on the other side, but that it fell as the condition subsided.

PAIN

The disease is accompanied with subjective symptoms, especially excruciating pains of neuralgic type along the entire ophthalmic branch of the trigeminal nerve, at times radiating to other branches as far as the occiput and preceding the eruption, as a rule, by hours or several days. This interval, Pickard and Montgomery asserted, represents the growth and spread of the virus along the nerves, which has not as yet reached the ganglion. The neuralgic pains manifest themselves in all degrees of intensity. Deep-seated, intermittent pains of definitely neuralgic type and of periodic character may exist with superficial distress provoked by irritation of the skin. The pain may assume the form, at times, of an exceedingly violent cephalalgia, occasionally with

ocular, supraorbital, retro-orbital or oculotemporal pain. The severity of the pain and the extent of the lesion bear no relation to one another. The greatest pain often is experienced when the cutaneous lesion is but slightly evident. In some cases nothing seems to relieve the torture. Rea suggested that this refractory pain is probably due to a lesion in the pons, since cutting of the sensory root does not relieve the pain.

The whole cycle lasts several weeks. The pain continues throughout the course of the illness and may last for years in the graver forms of the disease. Occasionally exacerbations occur after the disappearance of the zosters, while at other times the attacks of pain gradually become less severe; in any event, the pain is distressing because of its tenacity and reacts profoundly on the general condition of the patient. In elderly people, the distress may end only with the termination of life. The continuous after-symptoms have sometimes led to suicide. Forget reported such a case. In the aged, the pain may lead to severe prostration, and it has been responsible for exhaustion and death, as reported by Jeffries, in 1869, and by Doggart, in 1933. All authors agree that, after the eruption, pain is incontestably the most important symptom of the disease.

In most cases, after decrease in severity of the main symptoms, there is reduced sensitivity or a feeling of numbness over the affected areas for a long time. In some cases, even years after an attack, exposure to cold air, wind or rain produces a tingling sensation in the skin, and at times the most intractable postzosterian pains are observed. Rea reported the case of a man who suffered severely six months after an attack, and Mules described a case in which the pains were so violent that the patient had applied carriage varnish to the skin of the scalp. This caused severe dermatitis of the face and lids and the skin finally sloughed over the forehead to the pericranium. Some patients have pain with headache and vomiting, simulating the symptoms of meningitis. This may be due to involvement of the meningeal branch of the ophthalmic division, which sends filaments to the tentorium before the nerve reaches the sphenoid fisure.

Anesthesia of the cornea may also occur, and on this subjective basis of insensibility there may be superimposed persistent pains, often severe, especially during the first few days of the disease, and the pains may be particularly persistent in the aged. Herpes zoster in children is different from zoster in adults as far as pain is concerned. In the child the pain is less severe, rarely continuing beyond the period of eruption.

VESICLES

Herpes zoster ophthalmicus is an infectious disease of the nervous system characterized by the appearance of erythematous plaques on an edematous area of the skin and followed by the formation of yellow vesicles, discrete or in groups, along the terminal ramifications of the fifth nerve. In some cases the eruption may be extensive but never spreads beyond the median line. The vesicles vary in size, are irregular and may occur in small or large groups, which are scattered or confluent, with a tendency to coalesce. They may appear simultaneously or at different times, in the temporal region, the forehead, the scalp, the nose or the upper lid, and the eye itself may be involved. The vesicles at first contain a clear yellow fluid, which in a few days becomes cloudy. The erythema of the skin gradually disappears, and the vesicles soon become modified in character. They may become purulent or hemorrhagic, even gangrenous at times, in some cases resulting in extensive loss of the skin. This is probably due to the virus, with edema and swelling of the sensory nerve, to the severity of the disease or to secondary necrotizing infection, which in some cases may assume considerable importance.

As a rule, after a few weeks the vesicles dry up and leave a characteristic black crust, of irregular outline, which gradually falls off, leaving the skin in an anesthetic state and very tender. Scarring of the skin usually occurs, especially if the lesions have been hemorrhagic. The blebs leave indelible scars, characteristic, slightly depressed, pale, white cicatrices of the skin, and their typical distribution often renders possible a retrospective diagnosis of previous herpes zoster.

These erythematous plaques are essentially distinguished by the fact that their site corresponds to the cutaneous region of the fifth nerve. The disease is not always localized in the skin but may attack also the mucous membrane, that is, the nasal mucosa, resulting in mucopurulent coryza, or the ocular conjunctiva, causing redness and discharge. Lesions have been found within the nose and mouth, and limited to these membranes, by Fournier.

The vesicles of ophthalmic zoster are usually smaller and more numerous than the vesicles of zoster on other parts of the body. In some cases papules, bullae and pustules may appear instead of vesicles.

The inflammatory period of herpes zoster ophthalmicus is from eight to twelve days, although the ulceration of the skin takes a long

time to heal. In cases of the mild form the lesions leave pigmented spots or scars in five or six weeks, but in cases of severe type many weeks may elapse before the inflammation disappears and healing is complete.

The cutaneous manifestations, in order of appearance, are: hyperalgesia, erythema, vesiculation, rupture of vesicles, cicatrization and hyperesthesia.

The extent of the eruption varies a good deal and is almost always confined to one side of the face. Vesicles never extend across the midline except in the case of bilateral herpes zoster, which may or may not be of simultaneous occurrence. This overlapping of the midline has been reported in several cases; but it was probably due to an erythema of the skin with edema, and the eruption was not vesicular in type. Lewis stated that the eruption might extend over the midline because of overlapping of nerve filaments from the opposite side and because the distribution of the fifth nerve is often different on the opposite side. A typical zoster without eruption but with neuralgia may occur.

LYMPHATIC GLANDS

The lymphatic glands adjacent to the affected areas are practically always enlarged, and the adenitis may appear at times before the eruption. Ramond and Lebel stated that this adenopathy merits equal rank with the pain and the eruption of the disease, as it renders possible the differentiation of true zoster from a zosteriform eruption. Involvement of the lymph glands is almost always unilateral, is independent of all secondary infection and may be associated with the slightest eruption. The enlarged lymphatic ganglions are those whose afferent lymphatics are derived from the affected zone.

The adenitis is characterized by swelling and pain in one or more definitely movable ganglions and is often unrecognized unless the superficial ganglions are involved. The number of affected ganglions varies. There may be only one, but several are frequently encountered. In cases of herpes zoster ophthalmicus the preauricular gland is enlarged, and sometimes there is subangulomaxillary adenopathy. The submaxillary and subhyoid ganglions are involved in cases of superior or inferior maxillary zoster. The tumefaction may be seen, but most frequently it is recognized only by palpation. The skin over the swelling never shows any change in color unless the gland becomes infected from the vesicles. Pain is elicited by pressure and is not spontaneous, and it is far less severe than the pain of acute inflammatory adenitis with a tendency to suppuration.

Primary adenitis must be distinguished from secondary, or late, adenitis. The secondary adenitis is due to infection of ulcerated vesicles, with a tendency to suppuration and modification of the adjacent skin; but the mode of production of the primary type is still undetermined. It is possible that it may be caused by the virus of herpes zoster, although most investigators associate it with the cutaneous lesions.

Francois, in 1936, reported 2 cases of herpes zoster ophthalmicus in which preauricular adenopathy preceded all cutaneous eruption by three days. He stated that this observation afforded 2 examples of an atypical zoster and served to confirm the assumption that a primary preeruptive adenitis exists with zoster, and hence elucidated the still obscure pathogenesis of zosterian adenitis, namely, that it is caused directly by the zoster virus, which acts simultaneously but independently both on cutaneous nutrition and on the nutrition of lymphatic ganglions. He stated that it is more than probable that posterior poliomyelitis is the initial lesion and that this process acts on lymphatic ganglions, either indirectly, through lesions of the skin, or directly, simultaneously and independently, on cutaneous nutrition, there to produce incipient tumefacient degeneration of epidermis cells, and on the nutrition of lymphatic ganglions, to occasion the simple congestive hypertrophy of these glands. Cuénod and Nataf, Metz and Achard concurred in this opinion, and each reported cases. Other cases have been noted in the literature by Danlos, Barber and Steffan.

Primary zosterian adenitis exhibits its greatest tumefaction and sensitivity at the outset of the eruption, and occasionally even before eruption, then gradually diminishes in severity and finally disappears about the tenth or the twelfth day. Recovery by spontaneous resolution constitutes the natural and regular termination of this adenopathy. The gland never suppurates; the process never progresses to chronicity, and the prognosis is favorable. However, all adenopathy occurring in the course of the disease is not of zosterian nature, and all herpes accompanied with adenitis is not herpes zoster.

EYELIDS

In practically all cases, the eyelids are swollen and attended with redness, edema and some induration. The swelling involves particularly the upper lid, the loose cellular tissue of which is readily distensible. Sometimes the eyes are closed, and some exudate usually appears between

the lids. The hyperesthesia may be so great that it is almost impossible to open the lids, especially during the acute stage. Early in the disease ptosis is often present, which may be due to mechanical edema or paresis of the sympathetic fibers to the levator muscle, with mydriasis and paralysis of accommodation, or sometimes with paralysis of the internal rectus muscle or other third nerve palsy. The pseudoptosis which results from edema of the upper lid protects the cornea, and less opportunity is offered for the development of keratitis. Palpebral zoster frequently pursues a course far more serious than zoster of other parts of the body. Involvement of the lower lid offers a more favorable prognosis than that of the upper lid, since hyperemia, edema and vesicles are less severe. Zoster of the upper lid may be serious; and the older the patient, the more its complications are to be apprehended. Tacke, in 1903, reported a case of zoster in a young male in which the entire upper eyelid was covered with vesicles. These underwent suppuration, with resulting deformity of the lid. Carré reported a similar case. Clarke described a case in which the attack of herpes zoster caused destruction of part of the upper lid, exposing the cornea, with resulting corneal perforation. F. A. Phillips, in 1907, cited a case of zoster in a man of 47 years. The blisters of the lids took seven months to heal, resulting in a cicatricial entropion. Barré, in 1924, described a case of zoster with blepharospasm in a female. The author concluded that the determining cause of the reaction lay in the existence of zoster of the internal nasal branch and that there was a partial zona, which is often difficult to recognize. As a rule, however, these disturbances disappear with the termination of the eruption and in general do not indicate a grave prognosis. However, in some cases the ptosis may remain indefinitely after recovery from the disease.

CONJUNCTIVA

When the eruption is at its height, conjunctival injection is usually seen, with increased secretion. The conjunctiva is implicated primarily by vascular injection and tumefaction, as with practically all inflammatory disorders and other forms of irritation of the eye, and the bulbar, as well as the palpebral, portion is involved. Sometimes the conjunctival edema may cover the periphery of the cornea, and semipurulent secretion helps mask the conjunctiva.

Simultaneously with the appearance of the initial eruptive elements, vesicles may form in the conjunctiva, although they are difficult to discern on account of swelling and injection. Sometimes small pustules may be seen in the conjunctiva, which run the same necrotic course, with scarring, or the vesicles may resemble phlyctenular conjunctivitis, with severe pain, photophobia and lacrimation. Scriven (1869), von Arlt (1871), Lagarde (1874) and Sichel (1871) reported cases in which vesicles appeared on the conjunctiva. Wible, in 1917, described a case with conjunctival vesicles, which was the fourth case he had seen in 20,000 cases of disorders of the eye. Stieren, in 1906, reported a case in which many vesicles were present in the conjunctiva of the upper and lower lids. Pfingst cited a similar case. Kreibig, in 1938, described a case with bilateral conjunctival vesicles. Buhnemann, in 1937, described a case in a man aged 65 years. The conjunctiva of the left eye, near the outer limbus, showed a nodule, surrounded with vesicles, which were not painful to the touch. The nasal third of the corneal epithelium was loosened and stained with fluorescein. In this case the symptoms involving the conjunctiva of the bulb dominated the picture. Cases of conjunctival vesicles have been reported by Griffith, Michel, Herve, Blachez, Cousin and Périsson, Terrien, Tikanadze, Kinnicutt, Duméry, Lauber, Würdemann, Schoeppe, Knowles, Aubaret and Mastier, Couyba, Armaignac, Strzeminski and others.

Complications involving the appendages of the eye are not particularly serious. Conjunctival lesions are often present; the eye is red, and there is a certain degree of conjunctivitis with moderate edema in nearly all cases. Sometimes the conjunctival injection may precede the formation of the vesicles on the skin and often persists long after the disappearance of keratitis.

OCULAR COMPLICATIONS

Ocular complications, if any, may be observed in the various phases of herpes zoster, from the first day of onset to a remote date, even months after the healing of all cutaneous lesions. Early investigators stated the belief that complications were nearly always secondary to cutaneous manifestations and observed that inflammation of the eye occurred most often when the eruption was at its height or in the period of subsidence. The most dangerous complication of herpes zoster ophthalmicus, as well as of zosteriform or of secondary eruptions, is extension of the process to the globe of the eye. This occurs in about 50 per cent of cases, causing disturbances in the transparent media, the iris, the sclera, the cornea or the muscles. Hybord observed such complications in 45 per cent of cases; Hutchinson, in 36 per cent; Pacton, in 68 per cent; Koch, in 55

per cent; Buhnemann, in 50 per cent; Worster-Drought, in 50 per cent; R. F. Moore, in 60 per cent; Achard, in 60 per cent; Gundersen, in 50 per cent, and Rollet, in 75 per cent. Involvement of the cornea is observed in practically one third of all cases of ophthalmic zoster, a complication which enhances the gravity and often governs the prognosis of the disease. Spicer (1907) found this complication in 25 per cent of cases; Cantonnet, in 35 per cent; Paton, in 35 per cent; Agnello, in 40 per cent; Cohn, in 25 per cent; Hybord, in 43 per cent; Achard, in 35 per cent, and Wilbrand and Saenger, in 35 per cent. I found it in 35 per cent of 2,250 cases.

CORNEA

Corneal Anesthesia.—The corneal eruption is usually preceded by a period of insensitiveness, which renders possible the anticipation of keratitis. Corneal anesthesia should always be looked for, since it invariably entails the possibility of grave ocular complications. The anesthesia may occur simultaneously with the eruption or may appear with the subsidence of the herpes zoster. It is usually transitory; and recovery of corneal sensibility takes place during a period of months, or it may take years. In certain instances anesthesia of the cornea, appearing without a lesion of that membrane, constitutes the only symptom of corneal zoster. Mere anesthesia of the cornea, with dryness and impaired vasomotor reaction, cannot be regarded as the essential factor in production of the keratitis. In testing for corneal sensitivity, most investigators have used the hair apparatus of von Frey. Pflimlim stated that the threshold of sensitivity of the normal cornea showed a value of from 5 to 10 Gm. per square millimeter for recognition of contact and of from 10 to 20 Gm. per square millimeter for sensation of pain.

Keratitis.—The cornea is often affected during the course of the zoster and is the seat of the most serious ocular manifestations. Many forms of keratitis present themselves. They may be ulcerative, superficial or deep; nonulcerative, superficial or deep, or a combination of these forms. In the early stages, there is little, if any, infiltration, and the vesicles are easily overlooked, as examination is difficult because of the irritation and blepharospasm.

Keratitis, the essential lesion, consists of a subepithelial infiltrate composed of round, discrete, opaque dots. These dots are most numerous in the substantia propria but may be seen at lower levels. As a rule, the corneal involvement appears at the height of the evolution of the herpes zoster, on the sixth or seventh day.

Cases have been noted in the literature in which the initial lesion was a keratitis. This reversal of form is exceptional, for it is rare that keratitis precedes the cutaneous eruption. Pflüger, in 1874, reported the first case. In Terson's case keratitis developed two weeks before the cutaneous eruption. Similar cases have been reported by Doggart, Veil, Valière-Vialeix, and Bussy and Bonamour. Ahlström, in 1904, described an unusual case in which corneal zoster was the only form of involvement of the fifth nerve in the course of zoster of the lumbar plexus. Von Hoffmann, in 1879, described a similar case, but without the cutaneous eruption.

It is customary to consider two forms of keratitis as occurring in the course of herpes zoster ophthalmicus, aside from the accidental complications. One form is characterized by the occurrence of groups of minute, transparent vesicles, resulting from elevation of the epithelium and situated usually at the nasal periphery. The other form is characterized chiefly by the invasion of the deeper parts of the parenchyma or the interstitial tissue, without vesicular eruption or effect on the epithelium. Some authors claim that superficial lesions are exceptional, and since their appearance is rarely detected, their existence has been questioned by some investigators. J. Rollet, in 1932, stated that he had never observed this superficial form. He expressed the belief that there was only one form of keratitis and that interstitial lesions were constant, as in the skin. However, superficial vesicles do occur, and they have been demonstrated in many cases; but deeper infiltrates may appear in the course of the disease, with or without any superficial lesions. Epithelial edema is a constant factor.

Parsons, in 1912, stated that most herpetic lesions were superficial, while Paton, in 1926, concluded that the majority of corneal lesions consisted of deeper corneal infiltrations and that the subepithelial infiltrate was the initial lesion. Wangler stated a similar opinion in 1889 and reported 6 illustrative cases.

The corneal vesicles, if present, are usually multiple and may appear in groups and rupture, leaving small, shallow areas of ulceration, which tend to coalesce and leave crenated borders. These small ulcers usually heal rapidly and may be followed by fresh crops of vesicles, or the ulcers may enlarge and fuse, leaving a large, cloudy area of denuded epithelium. Secondary infection may occur, forming deep central or peripheral ulcers, which may result in perforation. Corneal denudations have a variable result. A simple ulceration may leave a leukoma, while

other ulcerations may leave numerous nebulas. Some opacities always remain, and pannus may develop. In some cases the vesicles may be accompanied with deep corneal infiltrates without ulceration, while in others the corneal vesicles develop without perceptible corneal infiltration. Irregular, gray opacities are noted at various depths, with haziness and edema, which may or may not be preceded by vesicular eruption. The corneal infiltration may precede the vesicular eruption in the cornea and in the skin and may heal with it, leaving as a sequela a more or less dense zone of anesthesia.

Descemet's membrane may show folding. Paton asserted that this was due to hypotonia, while Doggart claimed that it was the result of keratitis. Rollet stated that either the deep striae in the cornea were due to the folds in Descemet's membrane or they represented dehiscences between deeper layers of the stroma. Cloudiness of the cornea was noted in connection with these folds. Precipitates on Descemet's membrane have appeared frequently but are often difficult to see without the slit lamp. Rollet reported a case in which the cornea was involved, and examination with the slit lamp showed numerous striae at different levels of the cornea, with considerable precipitation on Descemet's membrane. The iris was normal, and there were no synechias.

Deep corneal infiltrates may appear, which may or may not leave a permanent scar, and deep infiltrates may form which do not undergo purulent disintegration. Often ulceration occurs, which may be compared to that of neuroparalytic keratitis following section of the trigeminal nerve, that is, it develops slowly, without any tendency toward spontaneous cicatrization, extends gradually, is accompanied frequently with interstitial infiltration and later may leave a dense leukoma. Paresis of nerves may remain, and neuroparalytic keratitis may occur. Cases of this complication have been reported by Cross, Ginsberg, Jacqueau, Gillette, Kroll and Hybord. In the cases reported by Lafon and Villemonte the neuroparalytic keratitis developed six weeks after the onset of the herpes zoster. However, neuroparalytic keratitis does not necessarily always occur with paralysis of the sensory root. Clinical results suggest that it is a symptom of irritation, and not the result of paralysis of the sensory division. The nutritional state of the fibers of the fifth nerve depends on the cells of the gasserian ganglion. Fibers beyond the ganglion degenerate if separated from the ganglion by disease. This degeneration usually means keratitis and loss of the eye, and the keratitis occurs during the active process of degeneration of the nerve fibers. Redslob expressed the belief that corneal opacities observed during herpes zoster not only represent disturbances of neuroparalytic character but constitute the true eruptive foci.

Deep corneal infiltrates may form which are similar in clinical appearance and course to disciform keratitis. Cases have been reported by Cross, Neame, Wangler, Sulzer, Wilbrand and Saenger, and Schenkl.

Parenchymatous keratitis may occur at the onset of herpes zoster ophthalmicus as a complication, or it may appear frequently as an end result of corneal vesicles. The vesicles on rupturing induce a superficial ulceration, which, in turn, may produce keratitis. The infiltration is not due to corneal ulceration, and the epithelium of the cornea remains intact. The majority of authors describe parenchymatous keratitis as a rare complication. It is assumed that this keratitis results from an epithelial erosion which the corneal vesicles leave after rupture, and keratitis without epithelial lesions is said to be exceptional. However, Valière-Vialeix opposed this view. In a study of 17 cases, he observed interstitial keratitis in 13, in 5 of which epithelial lesions were present; but he concluded that the superficial lesions were secondary, or at least that the superficial and the deep lesions appeared simultaneously. He stated that parenchymatous keratitis is the form customarily and most frequently associated with herpes zoster ophthalmicus and that, in any event, lesions of parenchymatous keratitis do not represent the end result of superficial lesions, in consequence of a gradual extension. He concluded that the two forms of keratitis were independent lesions, two different localizations of the zosteric infection, and that they have an independent evolution, namely, corneal vesicles and parenchymatous keratitis. Satanowsky, in 1931, reported 2 cases in which there was no superficial involvement of the cornea. Similar cases have been described by Koster, Ahlström, Leopold, Moret, Rollet and Grand-Clément, Schiess-Gemuseus, Ginsberg, Tsĭekhanovich and Márquez.

Holzer reported an unusual case of corneal opacity following herpes zoster ophthalmicus. One year after an attack an irregular circular opacity developed near the nasal limbus. The epithelium was intact, and corneal sensitivity was diminished. No cause could be found for the unusual opacity. The results of all laboratory tests were noncontributory, and physical examination revealed no abnormality. Gradually the opacity became less dense. Examinations with the slit lamp made at intervals disclosed at first a milky

appearance, with an irregular epithelial surface and many white deposits below. As the opacity extended, there appeared at the margins a dense line of yellow deposits. These deposits disappeared one month later. Folds in Descemet's membrane were observed, which later also disappeared. Lister reported a similar case of dense, spreading corneal opacity following herpes zoster. One year later the ulcer was 2 mm. in diameter, with smooth epithelium and good corneal luster. At no time was there any inflammation of the cornea.

Hypopyon and sloughing of the cornea have been reported in many cases, by Jeffries, Lacaussade, Calhoun, Noyes, Sommer, von Hoffmann, Spicer, Smith, J. Hutchinson, Da Fonseca, Elliot, Duméry, Teulon, Galezowski, Eyer, Adler, Lucic, Randolph, Hirschberg and others. In many of these cases, and in others, the corneal lesion has resulted in perforation and enucleation has been necessary. In the case of hypopyon reported by Klauber, in 1918, there was no corneal infiltration, but iritis was present. Meller expressed the belief that disease of the trigeminus produced tissue defects within the iris, which led secondarily to necrotic foci; these, in turn, caused purulent inflammation.

Relapse of the corneal infection is common, for the damaged epithelium is unable to resist exposure and the vitality of the cornea is lowered. Serious ocular conditions may follow. A coexistent iridocyclitis and descemetitis may add to the decrease of corneal resistance. These lesions interfere with vision, ordinarily persist for several weeks and are a great source of annoyance to the patient. Diminution of vision due to paralysis of accommodation should be carefully differentiated from that which involves degeneration of corneal epithelium. Confusion is possible because this superficial ulceration of the cornea may at the onset be visible only with indirect illumination or after the use of fluorescein.

Localization of interstitial alteration of the cornea in a circular zone or in one section of the cornea constitutes a characteristic of herpes zoster ophthalmicus. Bonnet, in 1939, reported the occurrence of such localization in a male patient, on the third day after the cutaneous eruption. Anesthesia of the cornea was noted near 2 o'clock, localized in the superointernal sector; the rest of the cornea, on the contrary, was hyperesthetic. Later, interstitial disturbance manifested itself in the area of anesthesia; subsequently, minute vesicles appeared in this area and finally ulcerated. Descemetitis soon developed. Bonnet and Colrat noted the frequency of this limitation of the disease to one sector and stated that this topographic pattern in interstitial alteration of the corea was governed by the exclusive involvement of one nerve fiber of the cornea, namely, the fiber corresponding to the meridian affected. Guillain, Lagrange and Périsson, in 1926, reported a case in which the cornea was involved. Examination of the corneal reflex demonstrated that sensibility was intact in the central part of the cornea, the sensory innervation of which pertained to the ciliary nerves. On the contrary, the conjunctiva and the periphery of the cornea, to which were distributed the terminal branches of the ophthalmic nerve, were anesthetic, but no difference could be noted between zones innervated by these various nerve branches. Molter described the case of a female with opacity of the entire half of the cornea. Tests for sensibility revealed complete anesthesia in the region of the denser opacity of the cornea, with diminished faculty of sensation for contact and pain in other opaque areas, and diminished pressure sense and complete abolition of temperature sense in the areas of most marked opacity. It is conceived that certain ciliary nerves may be affected exclusively and that this limited involvement may present itself as an alteration in one sector of the cornea.

MODIFICATION IN OCULAR TENSION

Increased ocular tension may be classified as two types: the first comprising accidental occurrences of hypertension associated with iridocyclitis of zosterian origin, and the second involving acute or chronic glaucoma without iritis. It is questionable whether the latter type is due to zoster as a specific etiologic agent or whether, rather, it is due to a condition such as pneumonia or bronchitis, for these diseases are capable of precipitating glaucoma in a properly predisposed eye. The glaucoma is generally of acute unilateral type, on the same side as the eruption, and is characterized by dilatation of the pupil, pericorneal injection and severe pain. The increase in tension usually appears within fifteen or twenty days after the eruption, but rarely precedes it.

In the first form the rise in tension is probably due to involvement of the iris and the ciliary body, whether or not the cornea is affected. In an eye predisposed to glaucoma, herpes zoster is capable of precipitating an attack. Morax (1916) held that herpes zoster awakens a latent glaucomatous condition. This was seen in a case of glaucoma precipitated in the course of zoster of the first branch of the fifth nerve, without involvement of any structure of the eye, as reported by Dubois, in 1912. Weeks stated

that glaucoma following herpes zoster ophthalmicus was no doubt due to changes in the composition of the aqueous, which render it less diffusible and prevent proper filtration through the lymph channels at the angle, as lymph spaces do not easily tolerate foreign products. In many such cases of glaucoma following iridocyclitis atropine has been of benefit. Morax (1916) cited 2 cases of glaucoma secondary to iridocyclitis. Other cases have been reported by Knapp, de Schweinitz, Hirschberg, Clark, Parker, Woods, Lodge and Lodge, Elliot, Dubois, Erdmann, Rea, Weeks, Veasey and Königstein and others.

Sometimes the tension is high early in the disease, and later it is lowered. It is often lowered while the inflammation is subsiding. It is usually low when folds are seen in Descemet's membrane or when atrophy of the ciliary processes is present. When the ocular tension is determined throughout all periods of the disease, there are seen many variations, which are transitory and invariably fluctuate widely about the normal tension. Cases in which the tension is decreased have been reported by Horner, Maillet-Guy, Goldzieher, Horstmann, Achtermann and others. Sédan stated that hypotension occurs not only in connection with corneal lesions but with conjunctival lesions and is most marked with ulceration and vascularization of the cornea. He stated that hypotension was never encountered in the presence of an intact cornea. Rollet expressed the same view. Sasportas, in 1913, reported the case of a man aged 59 years. One week after the initial appearance of the herpes a large hemorrhage developed in the anterior chamber. The cornea was anesthetic. The iris was moderately dilated and failed to react to light, and at certain points it presented ecchymoses. The tension was elevated. Later the volume of the globe appeared to diminish and presented evidence of incipient phthisis. After a time the tension became elevated, and the globe recovered its normal volume.

In many cases the disease has been ushered in with acute glaucoma. Such cases have been cited by Bradburne, Kennon, Bane, Scott, Lewis, Haitz, Rollet, Bussy and Bonamour, Jacquet and Pantol. Brav reported such a case and expressed the belief that the increase of tension was due to zoster of the fifth nerve, as this nerve is a vasodilator and may cause not only hyperemia but stasis, which may give rise to acute glaucoma. Pierron stated the belief that hyperemia of the vessels accounted for the secondary glaucoma. Urrets Zavalia asserted that ocular hypertension is an initial symptom of herpes zoster ophthalmicus and recorded 2 cases. The glaucoma in these cases preceded the eruption by several days. There was no involvement of the cornea or iridocyclitis in either case. Colrat, in 1931, described another case in which the disease was ushered in with acute glaucoma.

Modifications of ocular tension are secondary. When hypertension develops in cases of interstitial keratitis, the tonus may increase until glaucoma is noted. On the other hand, when the tension is decreased, there is usually present an iritis, which changes the regulatory system of the eye, precipitating hypotonia, or even in some cases phthisis bulbi may develop. Symptoms resulting from these disturbances of tension may also be seen when inflammatory complications are not present or have disappeared. In such circumstances a direct action of the sympathetic nervous system is assumed.

IRIS

Next to the cornea, the anterior uveal tract is most frequently affected with herpes zoster. In most cases in which the cornea is involved some iritis is present, with contracted pupil and photophobia. In other instances a true iridic inflammation may develop, with intense pain, redness, miosis, disturbed vision and posterior synechias, leading sometimes to hypertension. Every case is characterized by a small pupil, the result of irritative reflex miosis, unless there has been a paralytic mydriasis, due to irritation of the ophthalmic ganglion, or posterior synechias, due to the presence of plastic exudate. In some cases degeneration of the iris results, followed by atrophy of the ciliary processes and phthisis bulbi. Heterochromia may gradually develop at times. Cases of this type have been reported by Genet, Federici, Igersheimer, Viallefont and others.

The iritis may not appear until late in the course of the disease. Cases of this type have been cited in the literature by Paton, Kosminski, Horstmann, Michel, Wyss and others. Or the iritis may appear at the same time as the keratitis, as reported by Sattler, Noyes, Koch and Cohn. Or it may occur when the corneal complications are subsiding, as described by Crisp, Rollet, Ishiwara, Huguet, Pacton, Chance, Martini and Sattler. In some cases the iritis may appear before the cutaneous eruption, as reported by Bussy and Bonamour, Gould, Johnen and Jorissenne. Iritis without preceding keratitis is exceedingly rare, but cases of this kind have been noted in the literature by Paton, Bowman, Satanowsky and Jelkovitch, Lafon and Villemonte, Machek, and Meller. Primary iritis, if undetected, may produce grave posterior syne-

chias. This form, Rollet stated, is latent and might be compared in its insidious course with precocious secondary syphilitic iritis. Gilbert, in 1921, mentioned 9 cases of primary iritis that he had encountered and reported 2 of his own. In his first case a man aged 49 was seen ten days after he first complained of severe pain in his forehead. Some conjunctival hyperemia was noted; the iris was steamy, and corneal anesthesia was present. Hypopyon developed, and blood was noted in it. During the next few months thirty-five small hemorrhages occurred in the anterior chamber. The tension gradually increased. Five years later the eye was enucleated. Gilbert stated the belief that the iris was often affected in this disease, not as a result of secondary spreading of the corneal process to the iris but as a genuine primary herpetic disease of the uveal tract, characterized by initial neuralgic pain and circumscribed swelling of the iris, with hyperemia and often with hemorrhage.

It is difficult to determine whether iritic hemorrhage is possible without previous inflammatory reaction, although Sasportas, in 1914, reported a case in which hemorrhage from the iris into the anterior chamber occurred without previous inflammation of the iris. Machek, in 1895, described in great detail a case in which hemorrhagic iritis developed. As a result of continual pain and a disturbed nutritional state, the man died two years later. The cornea was not involved. Tension was reduced. The pathologic changes in the iris began with neuralgic pains in the eye, followed by hyperemia and inflammation of the iris, with plastic exudate and resulting adhesions.

Swelling of the pupillary part of the iris with hemorrhage into the anterior chamber was termed herpes zoster of the iris by Machek, Gilbert, Verhoeff, Zeeman, Schoeppe and Löwenstein. Rollet stated that actual zoster iritis often pursued a chronic course. If it was acute, the patient usually became extremely ill, in consequence of the intense pain and headache, and was often unaware of the disease of the eye. In addition to this genuine type of zoster iridis, Rollet defined profound iridokeratitis, with or without increase of tension, in which the anterior corneal epithelium is completely intact and the opacity is interstitial.

Meller asserted that the focal areas of hyperemia with the iris were not due to vasodilator phenomena directly but, rather, resulted from inflammatory reactions brought on by destruction of tissue. The theory of trophic disturbance must be abandoned, as removal of the gasserian ganglion frequently has not led to disease of the iris.

SCLERA

Scleritis is a rare complication of herpes zoster ophthalmicus and usually occurs late, in association with keratitis or iridocyclitis. The scleral nodules are small, circumscribed, red, painful areas with translucent centers. The conjunctiva over them is smooth and congested and may be adherent. After many weeks, or sometimes months, the nodules become smaller, without ulceration, and leave a slate blue discoloration of the sclera. The iris often becomes atrophic nearest the nodules in the sclera. The pupil may be inactive or may be dilated. Relapses are common, and fresh nodules arise in areas of the sclera hitherto unaffected. Cases have been reported by Kendall, Lauber, Mayou, Stellwag von Carion, Thompson, Meller, von Hoffmann, Penman, Jeffries, Clavelier, Strzeminski, Sourdille and Legrand, Fassbender, Doggart and Goldberg. Genet reported several cases, and in 1 of them a similar eruption appeared in the other eye four years later. Verderame, in 1913, described a typical case of this complication in a woman of 54 years. The left frontal region, the left side of the nose and the region of the external commissure of the left eye showed extensive involvement of the skin. The preauricular glands on the left side were congested. The globe was injected, with punctate keratitis. Six weeks later perikeratitic injection was pronounced. The sclera exhibited two elevations, of a reddish violet color, which were painful on digital pressure. At this time ocular tension increased and posterior synechias were present. Six months later the orbital pains had disappeared. The sclera exhibited two areas, of a slate red color, which at this time were painless on pressure, and ocular tension was reduced to normal. Terrien, in 1900, reported an interesting case of a woman of 59 years, in which there was first noticed in the superoexternal part of the scleral region a red, infiltrated, painful area of episcleritis. This soon spread to the cornea and presented a diffuse infiltration, which extended to the pupillary area. The corneal eptihelium remained intact. The pupil was contracted and reacted faintly to light. About ten days after the ocular involvement an eruption of vesicles appeared over the left frontal region, preceded for two days by intense pain over the entire left side of the head. This case, again, emphasizes the occurrence of primary ocular manifestations, as an initial symptom of herpes zoster, several days before the cutaneous eruption.

INVOLVEMENT OF THE NASAL NERVE

Ocular complications of herpes zoster are particularly frequent when the eruption invades the territory of the nasal nerve. The form which is generally confined to the anterior segment of the eye is most often characterized by an eruption of vesicles on the anterior surface of the cornea. Bowman, in 1869, and Hutchinson, in 1869, stated the opinion that the cornea is never involved unless the nasociliary nerve is affected, but Vernon, Coppez and Cohn found exceptions to this rule and noted, also, that when the nasociliary branch was affected the cornea was not always involved, as in cases reported by Douglas, Jeffries, Moers and Wadsworth. Hybord modified the rule expressed by Bowman and Hutchinson by stating that the cornea and iris are rarely affected unless the dermal eruption occurs in the region supplied by the nasociliary nerve, but that they are usually involved if the entire side of the nose, or the ala nasi alone, is covered with vesicles. Hybord, in 1872, reported 53 cases in which the tip of the nose was involved, in 35 of which ocular lesions were present. Ahlstrom, in 1904, submitted 50 cases. The cornea was affected in 23 and the nasociliary nerve in 20 cases. In 3 cases the cornea was involved, but the nasociliary nerve was not disturbed. Teulières and associates, in 1933, asserted that invasion of the internal nasal nerve is always accompanied with lesions of the cornea.

The worst ocular complications of herpes zoster ophthalmicus are generally associated with vesicles along the nasal nerve. While it is generally assumed that involvement of the nasal branch entails the hazard of ocular complications, numerous observations have shown that iritis and corneal scars may occur when the nose is free from eruption and, conversely, that these ocular complications may fail to appear when zoster has attacked the root of the nose and the side of the nose all the way to the tip. Instances in which eruption covers the entire side of the nose without affecting the eye are explained by involvement of the ramifications of the second branch of the nerve. Wadsworth attributed the distribution in a case in which the tip of the nose was affected but the cornea remained clear to an anatomic anomaly, described by Turner, in which a small supratrochlear branch of the frontal nerve joins the infratrochlear branch of the nasociliary nerve. In such a case the herpes zoster confined to the frontal nerve includes the nose but not the eye. Disease of the globe, with absence of eruption on the nose, is attributed to alteration of the single ocular portion of the oculonasal nerve, whose course is endonasal but becomes external only in the inferior portion of the nose. As a general rule, the eye scarcely ever suffers much when the nose is not affected, and the severity of the eruption on the nose is usually in direct relation to the severity of the ocular symptoms. But it does not follow that the eye is exempt when only the forehead exhibits eruption of vesicles. Rollet observed ocular lesions with zoster frontalis as well as with zoster lacrimotemporalis.

In many cases the lacrimal nerve is involved, and vesicles may appear on the skin of the lids, the conjunctiva and the side of the nose. It is often difficult to tell whether or not the lacrimal nerve is affected unless there is a great deal of eruption on the upper lid, with edema and injection of the conjunctiva. The fibers of this nerve run alongside the frontal nerve.

DISTURBANCES OF THE SYMPATHETIC NERVE SUPPLY

In cases of ophthalmic zoster disturbances of the sympathetic nerves may assume the form of the Claude Bernard–Horner syndrome, and the complex has been reported in some cases, with enophthalmos, contraction of the palpebral fissure and miosis. Typical cases were described by Aubaret and Morenon, in 1927. In 1937 Federici reported a similar case. He stated the belief that in this case the virus of herpes zoster ascended the nasal branch of the ophthalmic nerve and was transmitted by a fine branch of the sympathetic nerve, producing the syndrome. Jacquet and Bariéty, in 1926, reported the case of a woman of 32 years with corneal anesthesia, enophthalmos and diminution in size of the palpebral fissure but no miosis. Miosis rapidly developed after administration of physostigmine and persisted a long time. On the contrary, atropine induced only slow and gradual dilation of the pupil. The difference in the effect of atropine and physostigmine on the affected eye and that on the other eye was evident. This complex continued to exist for approximately three weeks after healing of the cutaneous lesions. Jacquet and Bariéty concluded that the condition was due to paralysis of the sympathetic fibers. Talkovskiy, Rollet and Colrat, and Spicer (1907) described cases in which dysfunction of the sympathetic nerve supply was the cause. Ligertwood, in 1927, reported a case in which there was a lesion of the sympathetic nerve, which paralyzed the dilator pupillae, and a lesion of the oculomotor nerve, which paralyzed the sphincter. The author concluded that the sym-

pathetic nerve supply was injured in an operation on the glands of the neck, previous to the present illness, and that the oculomotor nerve was involved as a result of the herpes, causing mydriasis and paralysis of accommodation. Potts reported a case of paralysis of the pupillary sympathetic fibers and the ophthalmic division of the fifth nerve following an attack of herpes zoster ophthalmicus. The pupil was contracted and did not dilate when shaded or when cocaine was instilled but contracted when stimulated with light. Rosnoblet reported 2 cases of the syndrome in consequence of spasm or paralysis of the sympathetic fibers. Leriche and Fontaine stated the belief that in man some sympathetic fibers with ocular destination leave the first thoracic ganglion to follow the vessels and that ptosis after section of the sympathetic trunk is an active phenomenon, as it can be exaggerated by irritation of the sympathetic chain or can be made to disappear by removal of a neuroma. Some of the musculo-orbital fibers must leave the cervical sympathetic chain below the superior cervical ganglion, as excitation of a neuron of this chain increases the ptosis after suppression of the upper cervical ganglion. Aubaret and Margaillan, in 1923, reported a case of the syndrome in a man of 70, with miosis and contraction of the palpebral fissure, which they attributed to involvement of the sympathetic fibers. They expressed the belief that the filtrable virus became lodged in the sympathetic ganglions, either orbital or of the cervical chain, and produced the concomitant syndrome of miosis and contraction of the palpebral fissure. Starobypinska and Sterling, Dufour and Urrets Zavalía cited similar cases. Anatomic investigations conducted on the spinal cord of patients with herpes zoster have revealed lesions of the anterior horns of the cord and lesions involving radicular ganglions and fibers of the posterior funiculi. As the sympathetic nerves have a close relation to the spinal cord, it is conceivable that they may be affected to some degree in the form of paresis of the sympathetic fibers.

ARGYLL ROBERTSON PUPIL

Pupillary disturbances of purely nervous origin, without resultant iritis, may occur in conjunction with herpes zoster ophthalmicus, and the Argyll Robertson pupil has been noted in several cases. The sign appears late, often months after the eruption, is unilateral and is seen on the side on which the zoster had appeared. Verhoeff, in 1919, described a case of the syndrome which he believed due to a lesion in the ciliary ganglion. Redslob, in 1923, reported a case in a woman aged 66. The left pupil was dilated and did not react to direct or indirect illumination but did react in convergence. He stated that this observation proved that convergence exerts a more powerful action than luminous excitation on contraction of the pupil. Lesions of the ciliary ganglion nullified the effect of photomotor excitation on the sphincter but were insufficient to prevent the more energetic action of convergence.

Genet, in 1925, reported a case of a woman of 56 years. The pupil of the left eye was in a state of moderate dilatation, with complete immobility to light. The pupillary paralysis followed the disease of the skin and was present one year later. He stated the opinion that it was due to a lesion of the ophthalmic ganglion, consequent on primary irritation of the ophthalmic nerve by way of the nasal root of this ganglion. Although it is impossible to exclude deeper causes of pupillary disturbances, either in the nuclei of the oculomotor nerve or at the base of the encephalon, since zoster itself may be a manifestation of lesions which reveal themselves later, Magitot concluded that the ciliary ganglion is the true motor center which controls constriction of the pupil and stated that any alteration of this ganglion during herpes zoster probably accounted for the pupillary disturbances. Aurand asserted that the pupillary irregularities were toxic in origin. Valière-Vialeix reported a case in 1931 and stated that only 2 cases of unilateral Argyll Robertson pupil following herpes zoster ophthalmicus had been reported. Cousin and Périsson described a case of a woman of 64 years. There was no corneal lesion, but conjunctival vesicles were present. The pupil did not react to light, although the reflex on convergence remained normal. Nothing in the examination of the patient warranted a suspicion of syphilis. The tests on the blood and the spinal fluid gave negative reactions for syphilis, and no clinical or biologic stigmas were present. Guillain, Lagrange and Périsson, in 1926, described in detail a case of the Argyll Robertson sign in a man of 51 years. The intrinsic motility was intact in each eye so far as it related to accommodation. However, on the right side, there was encountered complete pupillary inertia to luminous excitation, in contrast to conservation of movements associated with accommodation and convergence and of movements associated with opening of the eyelids. The Argyll Robertson sign, which was of recent appearance, could not be considered

syphilitic in nature. There was no history or stigma of this disease, and tests on the blood gave negative results. In repose there was no anisocoria. Under the influence of light stimuli the left pupil alone contracted. Convergence was accomplished by pupillary contraction, which was equal on the two sides; this response is not obtained in cases of anisocoria. There were no paralytic disturbances in the territory of the oculomotor nerve. The nonparalytic character of the motor disturbance of the right pupil was confirmed by the fact that there was no mydriasis or disturbance of the function of accommodation. Moreover, conservation of the synkinetic movement (enlargement of the pupillary orifices at the moment of opening of the lids) would argue against the existence of iridoplegia, for if there is paralysis of the iris this phenomenon is not present. Guillain and associates concluded that the pupillary phenomenon was due to a lesion of the ciliary nerve and of the ganglionic cells thereto attached. This served to confirm the existence of peripheral motor centers of the pupil, a local ganglionic center disseminated in the parenchyma of the iris, as in the choroid or in the ophthalmic ganglion. Ciotola, in 1936, reported the observation of this type of pupil in conjunction with herpes zoster ophthalmicus in a woman of 36 years. The right pupil was narrower than the left; it was vertical, with absence of photomotor reflex, although reaction to accommodation and convergence were present. Gradual and insufficient dilation of the pupil followed the instillation of atropine. He assumed the existence of an encephalitic focus between the pupillomotor path and the oculomotor nucleus. Satanowsky, in 1931, reported 2 cases of this pupil with no synechias. He stated the belief that the sign is due to an inflammatory process, which may impair the function of muscle cells, innervated either by the sympathetic or by the common oculomotor nerve, and leaves more or less extensive areas of atrophy. He discussed the reason for the failure of the pupil to react to light when the nerve is intact and the muscle retains its contractile function. He concluded that in pupillary disturbances of herpes zoster ophthalmicus there is only a manifest disease in muscular function and that an intense stimulus may produce contraction and that, since the accommodative stimulus is greater than the luminous, the impression of the Argyll Robertson pupil is created. Localization of the process in neurons intercalated between the nucleus of the common oculomotor nerve and the anterior quadrigeminal bodies is not in accord with his observations, in which pupillary reaction in convergence and accommodation is not entirely preserved. Moreover, existence of a partial reaction of the pupillary margin to light, which in one observation appeared a year and a half after the eruption, argues against localization of the lesion in the opticopupillary reflex arc, as in cases of tabes and progressive dementia paralytica. In explanation of the fact that the Argyll Robertson pupil does not always appear after severe iritis which has left numerous synechias, it is pointed out that this form of iritis is superficial, while the iritis of herpes zoster is deep and leaves no synechias. Milian and Chapireau, Wolff, Hermann, Genet, Herman and Zutt have described similar cases.

It is reasonable to assume that there is involvement of the muscles of the iris, due to lesions of the ciliary nerves and of ganglion cells attached to them. This is the result of implication of the ophthalmic ganglion or of local centers disseminated in the parenchyma of the iris. Redslob concluded that alterations of the pupil were due to inflammation of pupillary fibers in the ciliary ganglion and explained the disappearance of the pupillary reflex to light and the persistence of the reflex in convergence by the fact that fibers which conduct impulses of light were destroyed first. According to Redslob, it is reasonable to suppose that fibers which conduct afferent impulses for convergence would themselves be sooner or later altered. Redslob stated the opinion that this type of pupil following herpes zoster was transitory. Meller expressed the belief that ciliary perineuritis is pathognomonic of herpes zoster, since it is not present with such trophic disturbances as neuroparalytic keratitis, which produces high lesions of the trigeminus. Anatomic study of eyes affected with herpes zoster, acute iritis and the Argyll Robertson pupil is necessary to determine the relation between inflammation and infiltration of muscles of the iris.

SYMPATHETIC OPHTHALMIA

Occasionally, cyclitis is associated with iritis and may cause blindness and atrophy of the diseased eye and threaten the sound eye with sympathetic ophthalmia. Cases in which this complication occurred have been reported by J. Coppez, Noyes, Jeffries, Guérin and Sommer.

EXOPHTHALMOS

There occurs sometimes in cases of herpes zoster a transitory exophthalmos, with or without hypertension, a complication which accords

closely with the theory of sympathetic excitation. Exophthalmos, as a complication, has been reported by ten Doesschate, Vázquez Barrière and Voisin. They stated that the proptosis was due to stimulation of the sympathetic fibers. In the case reported by Vialeix, Prosper-Veil and Isnel the proptosis was believed to be due to inflammation of retrobulbar tissue. Carmody and Batignani described similar cases, and each stated a similar opinion. Viallefont reported a case of herpes zoster with cutaneous lesions of the upper lid, occasioning the formation of scabs, which prevented the closure of the lids, so that lagophthalmos was superimposed on corneal anesthesia. Blepharorrhaphy was performed, with excellent results. This association of corneal ulcer due to corneal anesthesia with mechanical lagophthalmos was regarded as noteworthy.

ZOSTER OF FACIAL NERVE

Trigemellofacial zoster is the involvement of the fifth and seventh nerves in the course of the disease. Approximately 110 cases have been reported in the literature, by Fuchs, Chance, Hunt, Vogel, Vargha, Eichorst, Murphy, Ironside, Montgomery, Murzin, Barré, Weill and Reys, and others. Most authors feel that a double lesion of two adjacent ganglions is involved, the gasserian and the geniculate. The clinical picture is that of facial paralysis, with vesicles on the ear and vesicles along the ramifications of one or several branches of the fifth nerve. All three branches of the nerve were involved in the case reported by Baldenweck and Degorce, in 1939.

The anatomic relations between the fifth and the seventh nerve render possible the understanding of some obscure types of ophthalmic zoster. The facial nerve is represented almost entirely by its motor root. Its sensory root is formed by the intermediary nerve of Wrisberg, which, by way of its intrapetrous course, enters the geniculate ganglion. Some sensory fibers extend beyond the last peripheral segment of the aqueduct and become involved with motor fibers of the trunk of the facial nerve. From that small collection of sensory fibers is developed the chorda tympani, which with the lingual nerve, a branch of the trigeminus, shares in sensory innervation of the anterior part of the tongue.

Powell reported a case in which paralysis of the right side of the face developed, with loss of taste on the right side of the tongue and a continuous tingling sensation on the right side of the tongue and throat, as low as the thyroid cartilage, indicating involvement of the fifth, seventh, ninth and tenth cranial nerves. The voice was weak and hoarse, and the right uveal cord was less responsive in phonation. There was partial anesthesia of the right side of the palate and pharynx. The facial paralysis improved at once after extraction of two dead molar teeth, and the voice and the tingling sensation in the throat and tongue immediately improved. Claude and Schaeffer, in 1912, described a similar case. Klippel and Aynaud, in 1889, collected 17 cases of facial paralysis with herpes zoster ophthalmicus. According to their observations, facial paralysis usually appears during the first days of eruption. It is unilateral and is situated on the same side as the zoster, and there is rarely any paralysis of muscles other than those of the face. However, cases in which ocular muscles were involved have been reported by Barrière, Letulle, Raynard, Heydeinann, Caspar and others. Caspar and Murphy each reported a case in which the facial nerve was affected on the opposite side. Paralytic complications of the third and seventh nerves imply extension of lesions to these cranial nerves, and the numerous anastomoses of filaments of the fifth nerve with other cranial nerves would explain these involvements of other nerves. Letulle, in 1882, reported a case of facial paralysis in a male. On the twentieth day of illness partial paralysis of the right facial nerve developed, affecting the superficial muscles but leaving the tongue and palate intact. Strübing, discussing this case, stated the belief that the facial paralysis was due to peripheral neuritis of the first branch of the fifth nerve and that peripherally the infective process spread to the fine anastomoses of the facial nerve. From here the disease process extended centripetally in the fibers of the facial nerve until the paralysis developed.

Association of facial paralysis with herpes zoster ophthalmicus is a relatively infrequent occurrence. Rollet remarked the rarity of its development. Voight contributed 1 case and assumed that a neuritis common to the fifth and the seventh nerve was the origin of the condition. Eulenberg stated the belief that zoster was essentially a lesion of the facial nerve and that the seventh nerve conducts fibers the particular excitation of which provoked the zoster. Ebstein asserted that there was no relation between the gravity of involvement of the fifth and that of the seventh nerve and no chronologic relation in disturbance of the different nerves and concluded that there could be no relation of cause

and effect in the involvement between these two nerves. Souquez concurred in this opinion and reported a case in which the cause of the paralysis of the seventh nerve had to be sought in zoster of the ear, which in his opinion is an indispensable factor in zosterian paralysis of the seventh nerve. It the case described by Verneuil the herpes zoster was preceded by facial paralysis by several weeks.

Facial paralysis is occasionally total, but more often it is partial. It is fairly frequent and almost always follows the eruption, if it occurs. Recovery is the rule.

PARALYSES OF OCULAR MUSCLES

Paralyses of ocular muscles are not exceptional in cases of herpes zoster and are not dependent on the severity of the pain or the gravity of the disease. The paralyses appear with greater frequency the closer to the cephalic extremity the zoster occurs, and they are encountered most often with cephalic zoster, especially with herpes zoster ophthalmicus.

Such paralyses which develop in the course of the disease are commonly observed when the infection involves the ophthalmic nerve. Inasmuch as herpes zoster has a higher incidence in elderly people, complicating oculomotor paralyses have a higher incidence in this group also. The motor complications usually disappear after a few weeks or months, but may persist for a long time after the cutaneous symptoms have disappeared. Zentmayer described a case in which the paralysis was present one and one-half years after the attack. The ocular paralysis usually appears later than the cutaneous eruption, occurring in the phase of scar formation. The paralysis may appear at the same time as the cutaneous eruption, as in cases reported by Gillet de Grandmont and Oliver. Desirat stated the belief that paralytic phenomena of the muscles never appeared before the cutaneous eruption, but Mittendorf, Saint-Martin, Letulle and Schiffer recorded cases in which the paralysis preceded the eruption. Sometimes the paralysis involves several nerves simultaneously, each of which may be individually implicated, either partially or totally. The question has sometimes been raised whether these paralyses are actually complications or whether they are merely concurrent disorders. Most investigators think they are complications because they appear in much the same manner in a large series of cases. Hunt, in a series of 158 cases, found ocular paralyses in 24, or 14 per cent. Worster-Drought, Désirat, and Lloyd and Elliott each observed ocular paralysis in 7 per cent of cases. Hybord found 5 cases of paralysis of the ocular muscles in 100 cases of ophthalmic herpes zoster.

Paralyses of ocular muscles occur presumably from extension of inflammation of the fifth nerve to the motor nerves as they traverse the cavernous sinus and the superior orbital fissure. Some authors have stated that the paralysis is due to an associated meningitis or to extension of the infectious process to the neuraxis, with production of a nuclear lesion, or to involvement of the motor nerves in the anterior horns of the cord, with resultant paresis of the muscles affected. Wyss, in 1871, observed hemorrhages in the muscles and concluded that the muscular paralysis was due to thrombophlebitis.

THIRD CRANIAL NERVE

The most common complication of the ocular muscles is total or partial paralysis of the muscles supplied by the third cranial nerve, with or without participation of the pupil. I found 96 cases of paralysis of the third nerve in the literature. Rosnoblet stated that these paralyses occurred most frequently from five to seven days after the appearance of the vesicles but that they might appear weeks, or even months, after the eruption. Mittendorf observed a case of oculomotor paralysis that preceded the eruption. Schiffer described another such case. Metz, in 1913, collected from the literature 50 cases of herpes zoster ophthalmicus complicated by involvement of ocular muscles. The third cranial nerve was affected in 32 cases. The paralysis was either total or partial, and the branches supplying the internal or the external ocular muscles or combinations of these branches were affected. About 25 per cent of paralyses of the third nerve were complete. Many cases of paralysis of this nerve have been described in the literature by Hunt, Valière-Vialeix, Essen-Möller, Ardouin, Silcock, Wallace, Brissaud, Burwell, Durnerin, Braun, Fage, Paton, Michel, Schlesinger, Mules, Vernon, Reynolds, Weber and Ginsberg.

In cases of internal ophthalmoplegia following herpes zoster, in addition to sensory loss, certain motor fibers are involved. In these cases the lesion must be in the ciliary ganglion. Bär, in 1925, reported the case of a man aged 30 with partial paralysis of the third nerve, involving fibers to the pupil and the levator muscle. Being of the opinion that herpes zoster was an infectious neuritis due to a specific organism, he traced the association of the third and the fifth cranial nerves to their connection by a communication in the region of their entrance to the orbit. Cases of internal ophthalmoplegia have been described by Rutter, Achard and Castaigne, Baranov,

Elliot, Aurand, Veil and others. Isolated paralysis of the pupils is frequently encountered and may be the only symptom. The pupil is dilated and does not react to light or in accommodation to distance. In a certain number of cases, involvement of the entire internal musculature is noted, and patients present, in addition to paralysis of the pupil, a paralysis of accommodation which impairs close vision. In these cases of paralysis of accommodation and paralytic mydriasis the disturbance may persist for a long time. Several hypotheses have been adduced in explanation of this association—among them, the conception of herpes zoster as an infectious ganglioradiculitis, the implication of a meningeal reaction as an etiologic factor and the recognition of the intimate relationship between the virus of herpes and that of encephalitis, with frequent assumption of participation of lesions of polioencephalitis in the production of these paralyses. Cases of paralysis of accommodation and paralytic mydriasis were reported by von Arlt, Berlin, Grandmont and Höfer. Horner and Hasner reported cases of isolated paralysis of accommodation, and Oettinger, Cohn and D. Sulzer each added a case of isolated paralytic mydriasis.

Only one branch of the third nerve may be involved, that which supplies the levator palpebrae muscle, and ptosis may result. Usually recovery occurs. Such cases of isolated paralysis have been reported, among others, by Blachez, Brissaud, Hutchinson, Baliña and Herrera, Tardy, Howard, Kirisaua and Wangler. Study of a series of cases reveals a number of such cases of isolated paralysis. In most instances unilateral ptosis on the same side as the eruption represents the initial symptom of paralysis. Rarely both levator palpebral muscles are implicated at the same time; if so, ptosis is more prominent on the side of the eruption. Ginsberg, Fouchard, Menacho, Cohn and Jacksch have reported cases. Valude and Gallois, in 1924, published a case of bilateral ptosis and paralysis of the left superior rectus muscle in a woman aged 78. In a case described by Brissard the ptosis was associated with hemiplegia. The ptosis came on several months after the vesicles and was permanent. Letulle cited a case of ptosis which preceded the herpes zoster by two weeks.

THIRD, FOURTH AND SIXTH CRANIAL NERVES

Numerous cases of paralysis of the third, fourth and sixth nerves simultaneously have been recorded. Voisin, in 1936, reported a case of a woman aged 73 in which the third, fourth and sixth cranial nerves were involved. The right eye was proptosed, and motions were limited in all directions. Contributions to the literature have been cited by Rebattu, Kuhn, Monnier, Decbaume, Bonnet and Isrel. Vázquez Barrière, in 1937, described a case of paralysis of these nerves in a man of 72 years. After the cutaneous lesions had cleared, some exophthalmos was noted, followed by complete ophthalmoplegia and complete facial paralysis. Seven months after the attack the ocular motility became normal and the facial paralysis disappeared. Similar cases have been described by Sellers, Königstein, D. Sulzer, Tacke, Barrett and Orr, Ginsberg, Hall, Silcock and Aubineau. In the case described by Mildenberger, in 1937, the first and second branches of the fifth nerve were involved. Dalsgaard-Nielsen, in 1935, reported a case of ophthalmoplegia complicated with acute glaucoma in a woman. Francois, in 1936, observed a case in which ptosis was present from the onset. The pupil was dilated and fixed, with no reaction to light or in accommodation. Similar cases have been recorded by Head, Patterson, Turner, Velter, Leplat, Vázquez Barrière, Batignani, Pergola and Viallefont. In the case reported by Higgens, the ophthalmoplegia came on ten weeks after the cutaneous eruption. Brissaud cited a similar case in which the ophthalmoplegia followed the eruption in three months. This author found that total paralysis of the ocular muscles occurred in 40 cases

SIXTH CRANIAL NERVE

Paralyses of the abducens nerve are intermediate in frequency between paralyses of the third and those of the fourth cervical nerve and usually appear a short time after the cutaneous eruption. Metz, in 1913, found that paralysis of the sixth nerve occurred in 8 of 50 collected cases of paralysis of the ocular muscles. Hunt found it in 6 of 24 cases of such paralyses. Numerous other cases have been recorded in the literature by Doggart, McCulloch, Stieren, Galezowski and Beauvois, Danielson, Peter, Paton, Patterson, Gosetti, Weidner, Langenhan, Raynard, Heydemann, Oliver, Goldschmidt, Heilbrun, Lockwood, Schiffer and others. I found paralysis of the sixth nerve in 47 cases.

FOURTH CRANIAL NERVE

Isolated transitory paralysis of the trochlear nerve represents a rare complication in the course of cephalic zoster. However, Traquair cited 5 cases of such a complication, and Metz, 4 cases. Other cases have been described by Hunt, Caspar, Silcock, Vogel, Sulzer, Grand, Lesser and others. A total of 21 cases of paralysis of the fourth nerve were found in the literature.

INVOLVEMENT OF FIRST AND SECOND BRANCHES OF FIFTH CRANIAL NERVE

Up to the present time, there have been reported 72 cases of involvement of the first and second branches of the fifth cranial nerve. The first cases were reported by Hutchinson, in 1865, and by Bowman, in 1867, and since that time many cases of this condition have been described in patients of various ages, males and females alike. In many of these cases there was a history of complications involving the globe and the ocular muscles. Cases have been reported by Chance, Head, Flemming, Hunt, van Lint, Caspar, LaChaise, Bryan, Carré, Halipré, Schumacher, Bradshaw, Jaclard, Fassbender, Passera, Eyer, Lauber, Duplay, Cohn, Chemolosoff, Johnen, Horstmann, Knowles, Ramond, Ginestous and others. In a series of 98 cases of ophthalmic zoster, Hybord found 8 in which the superior maxillary branch was involved. Pergola described a case of involvement of the first and second branches of the fifth nerve in a man, a typographer, with paralysis of the levator palpebrae, iridocyclitis, hyphemia and complete ophthalmoplegia, followed by glaucoma. Pergola stated the belief that the lead from the type was carried through the blood stream and had affected the gasserian ganglion, and that the inflammatory process had traveled upward, to produce a lesion of the mesencephalon. Mildenberger and Bézi described similar cases. Fourestier and Zangger each reported a case of bilateral involvement. Langenhan, in 1910, reported a case of involvement of these branches complicated by paralysis of the sixth nerve. Smith, in 1878, cited a case complicated with hypopyon, with eventual loss of the eye. Sicard, in 1905, observed a case following mumps. According to van Lint's statement, in 1927, "René LaChaise, in his Lyons thesis, of 1924, was able to assemble only 26 cases of this condition," but I have found 56 cases in the literature up to that date.

When the eruption is limited to two branches, it is the adjacent branch that is always involved. No case has been observed in which two remote nerve trunks, such as the ophthalmic and the inferior maxillary division, have been affected. Zoster involving two branches is known as partial trigemellar zoster.

INVOLVEMENT OF FIRST, SECOND AND THIRD BRANCHES OF FIFTH NERVE

Involvement of all three branches of the gasserian ganglion is occasionally reported. Twenty-five cases of such a disorder are described in the literature. The first case was reported by Schiffer and Wyss, in 1866. In cases of total trigemellar zoster, the ophthalmic, the superior maxillary and the inferior maxillary branch are involved, but there is also participation of the sympathetic ganglions, as evidenced by pupillary disturbances and enophthalmos. Head reported a case in which all three branches were involved, affecting both lids, the cheek, the mucous membrane of the cheek, the tongue and the tonsil. Other cases have been reported by Agnello, Vaughan, Gowers, Camus, Elliot, Düring and Huber, Murzin, Siméon and Denizet, and Baldenweck and Degorce. Zentmayer, in 1906, cited a case in which all three branches of the fifth nerve were involved, complicated with muscular paralysis. Similar cases were reported by Roelofs, Pergola, Paton and Scriven. E. Rollet and associates, in 1931, described a case of paralytic mydriasas in a girl of 10 years. R .M. Campbell, in 1936, reported a case in which there was bilateral involvement of all three branches of the fifth nerve in a boy aged 6 years. Campbell stated that there were 30 instances of bilateral herpes zoster in the literature to date, but that the fifth nerve was not affected in all cases. Cases were reported by Glaubersohn, Fordyce, Fox, Hutton, Burgess and Anderson. Spicer, in 1892, cited a a case of severe zoster resulting in keloid changes in the skin and in perforation of the globe. In the case reported by Murphy, facial paralysis was present. Gerson, in 1937, reported a case in which the zoster followed arsenical treatment. Griffith, in 1901, described a case of zoster in a man of 60 years in which all three branches of the right fifth nerve were involved. The eruption followed the course of the supratrochlear and the nasal branch of the ophthalmic nerve. Vesicles appeared also over the right malar bone, the upper lip and the chin, involving the temporomalar branch of the superior maxillary nerve, the labial branches of the infraorbital nerve and the mental branch of the dental nerve. The eye was congested, with vesicles in the lower cul-de-sac and edema of the lids. The cornea was cloudy and ulcerated, with iritis and posterior synechias. Teulières and associates, in 1933, described a similar case and concluded that involvement of the internal nasal nerve was always accompanied with lesions of the cornea.

BILATERAL HERPES ZOSTER OPHTHALMICUS

Jeffries, in 1874, was the first to report a case of bilateral herpes zoster ophthalmicus, in a woman of 64 years. Both corneas were affected,

and perforation of the cornea resulted on each side.

The disease is rarely bilateral, but other cases have been observed by Lallier, Samelsohn, Jaclard, Douglas, Lipschütz, Schiess-Gemuseus, von Bärensprung, Hebra, Thomas and Buckley, Jorissenne, Greenough, Myers, Grindon, Carré and others. Touraine and Baumgartner, in 1934, reported a case of bilateral herpes zoster ophthalmicus in a man of 56 years. The nasal branch was not involved, and the cornea was free; but the frontal and lacrimal branches were affected on each side. Similar cases were reported by Verco, Blachez, Sédan, Anderson, Jaclard, Fourestier, Fassbender, Tacke, Zangger and others. De River and Moore saw cases in persons with histories of syphilis. Gallois described a case of bilateral ptosis. Hallam, in 1897, reported a case of bilateral ophthalmic zoster in a girl aged 13 years. Kreibig, in 1938, treated a patient with severe bilateral herpes zoster ophthalmicus, which was followed by death in two days. G. A. Sulzer reported another case of severe ophthalmic zoster which resulted in bilateral optic neuritis. Habran, in 1877, described an interesting case of the disease in a pregnant woman aged 28 years. At the end of the ninth month of pregnancy pneumonia developed. Eight days after the termination of labor, typical bilateral herpes zoster ophthalmicus developed, involving the first and second branches of the fifth nerve. I found 44 cases of bilateral ophthalmic zoster in the literature.

RECURRENT HERPES ZOSTER OPHTHALMICUS

As a rule the disease occurs but once in a lifetime, but in some cases it has appeared more than once in the same person. Charcot, in 1859, published an account of the first case of recurrent herpes zoster ophthalmicus; in this case the disease followed a gunshot wound. Emmert, in 1870, reported 3 cases, 1 of a girl of 4 years. Carré, in 1875, described a case of ophthalmic zoster in a girl of 16 years with six recurrences on one side during a period of six months. The disease later became bilateral. Kaposi reported a case in which the eruption appeared five times within a comparatively short time. Drouet, in 1924, cited a case in a woman aged 54 with three recurrences in a period of eight weeks. In Nieden's case four recurrences occurred in a period of six years. Cases in which the same nerve has been affected more than once have been reported by Berger, Fox, Kopp, Jaksch, Singer, Couyba, Talko, D. Sulzer, Spaeth, Hermann, Cofler, Grindon, Cookson, Vörner, Cross, Hallam and others. Head and Campbell found 4 instances of recurrence in 400 cases. In several cases recurrence has resulted in enucleation, as described by Greenwood, Meller and others. Rollet and Colrat, in 1923, described the case of a man aged 45 who suffered from successive monthly eruptions of zoster in the territory of the left ophthalmic nerve. The ocular tension was 9 mm. The case was presented on account of the ophthalmomalacia associated with the ophthalmic zoster, which is a rare complication.

INVOLVEMENT OF THE OPTIC NERVE

The disease sometimes affects the deep membranes of the eye, and cases have been described by many observers in which retinal hemorrhage and degenerative retinitis, choroiditis, optic neuritis, papillitis, optic nerve atrophy and retrobulbar neuritis were present. In some cases, however, no previous ophthalmoscopic examination had been made, and it is questionable in these cases whether the lesions were secondary to the zoster or were present before the attack. However, inflammation of the optic nerve may complicate herpes zoster ophthalmicus and may manifest itself when the eruption appears or as an end result. It is postneuritic in type and may or may not heal without resulting atrophy.

The insidious character of herpes zoster ophthalmicus is apparent at times in optic neuritis, which develops with the characteristics of papillitis and may terminate in blindness or in great reduction of vision. This complication may be the only one observed in the course of the disease. An edematous neuritis is seen, and the disk has poorly defined contours. The vessels are congested and tortuous. The disk gradually becomes pale. The neuritis is more often localized in the eye on the side of the eruption, although both eyes may be affected.

Hebra, in 1870, was the first to report a case of bilateral optic nerve atrophy following herpes zoster. In this case delirium and diffuse encephalitis finally developed. Hubsch, in 1872, described a case of optic nerve atrophy in a man aged 52, who for many years had had chronic herpes zoster. Eruptions had appeared and disappeared in various parts of the body for a long time. Eventually there was a gradual diminution in vision in each eye, with subsequent optic nerve atrophy, which was ascribed to the papillitis, as a result of the continuous zoster. Coppez, in 1873, was the first to mention a case of opacities in the vitreous following herpes zoster, with choroiditis and retinitis. Later cases were described by Noyes, Tacke, Sattler and Haltenhoff.

Rollet and Colrat reported a case of optic nerve atrophy in a woman aged 70 years. There was paralysis of the left oculomotor nerve with marked papillitis, which they stated was caused by perichiasmal meningitis, although the papillitis was unilateral. Similar cases have been described in the literature by Gould, Sulzer, Bowman, Daguenet, Wangler, Paton, Veasey, Adams, Strzeminski, Sinclair and others. Aurand, in 1920, described a case of optic neuritis in a woman aged 75 which he concluded was due to an embolus or a thrombus of the central retinal artery. Absence of cardiac lesions warranted the assumption of obliterating endarteritis. He stated the belief that circulatory disturbances in the territory of the ophthalmic branch facilitated localization of obliterating endarteritis. He mentioned 2 other instances of occurrence of vascular lesions in association with herpes zoster recorded by André-Thomas and Heuyer, in 1912. Pierron stated the belief that the optic nerve atrophy and optic neuritis were attributable to strangulation in the vicinity of the scleral ring.

Cohn cited a case of optic neuritis which developed after healing of the cutaneous lesions. After three months there was a small concentric contraction of the visual fields, with some reduction of vision. Cabannes reported a case of optic neuritis in a man of 30 years. The fundus was pale; the arteries were small; the veins were engorged, and two small, flame-shaped hemorrhages were noted near the disk. Other such cases have been noted in the literature by Murzin, Antonelli, Löhlein, Hirschberg and Puech. Ahlström encountered 1 case of optic neuritis among 50 cases of ophthalmic zoster. Koch, in 1939, reported a case in a child aged 5 years, with retinal edema and exudates in the macular region. Silcock mentioned 2 cases of optic neuritis, with retinal hemorrhages in 1 and thrombosis of the retinal vein in the other. Genet reported a case in which the condition resulted in phthisis bulbi, and Scott saw a case in which complete retinal detachment occurred.

Focosi, in 1935, described a case of retrobulbar neuritis with a large central scotoma, which developed during the course of ophthalmic zoster. He attributed the neuritis to the zoster because the neuritis manifested itself in the same region and occurred simultaneously with the zoster and because the herpetic process provoked lesions of other parts of the eye—in the cornea and the iris. He expressed the belief that the process was transmitted by branches of the trigeminus nerve which reach the optic nerve by way of the ophthalmic ganglion.. This hypothesis was enunciated by Fage. Deutschmann, in 1924, reported a case in which large central scotoma was present and vision was limited to 1/200. Two months later atrophy of the nerve developed. The disk was pale and well defined. Serologic tests gave negative reactions. The teeth and sinuses were normal. The author concluded that the retrobulbar neuritis was herpetic and that the virus migrated from the nerve sheaths of the fifth nerve through the orbit to the optic nerve. Peter stated the belief that the neuritis was an extension of the herpetic toxemia from the uveal tract. The pathogenesis of neural involvement is still a matter of dispute.

INVOLVEMENT OF OTHER NERVES

Just as there are paralyses of parts at a distance in cases of herpes zoster, irrespective of the situation of the eruption, so motor nerves of the eye may be affected in the course of zoster of remote localization. Most unusual are the cases in which wide separation exists between the areas involved. It is probable that two ganglions are affected at the same time. Delens and Wangler cited cases in which ophthalmic zoster followed or preceded zoster in other regions. Morénas and Colrat observed a case of paralysis of the extraocular muscles which occurred during the evolution of a dorsolumbar zoster. A woman aged 65 years suffered from zoster in the inferior thoracic region on the right side. One month later she complained of diplopia. Examination revealed total paralysis of the right third nerve. The zoster pains and the ocular paralysis persisted until her death. They stated the opinion that a nuclear origin of the paralysis in question might be assumed. Bradshaw, in 1894, described a case of thoracic zoster in a man aged 42 years, who at the same time had a zoster eruption on the left side of the head, with vesicles of the upper lid and conjunctiva. Hutchinson reported a similar case. Barber, in 1919, saw an interesting case in a child of 6 years who entered the hospital with herpes zoster on the left side of the chest. Two days later a similar eruption developed on the forehead, lid and temple of the same side. Corson and Knowles reported a case of a woman in which an outbreak of zoster occurred over the right scapula and at the same time an eruption developed over the first branch of the right ophthalmic nerve. Ahlström, Anger and Buller each described similar cases.

Hemiplegia of pedúncular or alternate type is likewise encountered. G. A. Sulzer, in 1907, reported a case of zoster with paralysis of all the extraocular muscles. A few weeks later hemi-

plegia developed on the right side. The muscular paralysis soon recovered, but paralysis of the sphincter of the iris remained. Ironside, in 1933, described a case of a woman with corneal ulcer. Five weeks later right hemiplegia developed. MacGillivray, in 1931, saw a woman with ptosis and conjunctival injection following ophthalmic zoster. Three weeks later she complained of weakness in the right arm. There was no exaggeration of knee jerks, and Kernig's sign was absent. Later left hemiplegia developed. Wohlwill, Brissaud, Duméry, Grandclement, and Chauffard and Rendu described similar cases. Perrin, Kissel, Pierquin and Gayet reported a case of zoster complicated with hemiplegia in a man aged 68 years. Autohemotherapy was used, whereupon the vesicles dried up and became covered with crusts and then disappeared, leaving deep cicatrices. The erythema in the frontal area persisted and was complicated with pronounced supraorbital and palpebral edema. Pains became intensified, and diplopia followed. Three weeks after the onset progressive left hemiplegia developed. The paralytic symptoms of the left arm and leg required eight days to become established. Paralysis of the left side of the face of central type followed. The authors stated the belief that the coexistence of ophthalmic zoster and hemiplegia was due to an exclusive radiculoganglionic lesion and that it warranted the establishment of the theory of zosterian neuraxitis. They concluded that in certain subjects who present vascular fragility the virus of zoster might provoke the occurrence of hemiplegia, though incapable of doing so in the healthy subject.

In some cases zoster is distributed over several adjacent segments while only one spinal ganglion is involved, no doubt owing to the presence of communicating fibers. At times the disease may affect widely separated areas simultaneously. Couyba, in 1877, described a case of a man aged 65 in which the disease ended fatally. In this case there was involvement of the trigeminal, glossopharyngeal, facial, spinal accessory and hypoglossal nerves. Dennis reported a case in which the fifth, seventh, eighth and ninth cranial nerves were involved. Powell, and Baldenweck and Degorce described similar cases. Claude and Schaeffer saw a case in which involvement of the third, fifth, sixth, seventh and eighth nerves followed ophthalmic zoster. The authors stated the belief that the primary process was an acute poliomyelitis posterior, which spread to involve the spinal ganglions and their analogues in the brain stem, the gasserian and geniculate ganglions. The extension from sensory to motor nuclei occurs through the spread of a basilar infection by way of the subarachnoid space, a meningitic process being demonstrated by the leukocytosis of the spinal fluid.

FATAL CASES

In cases of ophthalmic zoster disastrous consequences sometimes follow this usually mild infection, to the extent not only of complete destruction of the eye but even of death. Many observers have reported a fatal outcome, among them Weidner, Wagner, Wyss, Aubineau, Brissaud, Doggart, Sunde, Bézi, Couyba, Howard and Wohlwill.

(To Be Concluded)

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Cornea and Sclera

KERATOCONUS POSTICUS CIRCUMSCRIPTUS. G. WISE, Am. J. Ophth. **27:** 1406 (Dec.) 1944.

Wise reports a case of keratoconus posticus circumscriptus in a man aged 24. The lesion appeared as a large, eccentric, nebulous opacity, occupying more than one-half the corneal area posteriorly. The anterior surface showed a normal curvature. The interesting features of the case were that the cornea was one-fourth the normal thickness and that the lesion stopped short of the limbus.

W. S. REESE.

CORNEAL DYSTROPHIES. R. VON DER HEYDT, Am. J. Ophth. **28:** 55 (Jan.) 1945.

Von der Heydt briefly describes "Bueckler's triad" of corneal dystrophies which includes the Fleischer, the Haab-Dimmer and the Groenouw and also describes Fuchs's epithelial, and Salzmann's nodular dystrophies and keratonus.

W. S. REESE.

THE USE OF CHOLINE IN CASES OF ULCER AND OF LEUKOMA OF THE CORNEA. T. J. DIMITRY and P. AZAR, Am. J. Ophth. **28:** 62 (Jan.) 1945.

Dimitry and Azar conclude that choline is a most promising agent in the treatment of ulcer and leukoma of the cornea and that it should be applied topically.

W. S. REESE.

A CASE OF CORNEA PLANA. C. COCKBURN, Brit. J. Ophth. **28:** 486 (Oct.) 1944.

The condition of cornea plana was seen in a Greek soldier, aged 28. Visual acuity had always been poor, although, significantly, he stated that it had deteriorated since enlistment, one year previously. The refractive error for the right eye was + 10.50 D. sph. ⊂ + 1.50 D. cyl., axis 60, with visual acuity of 6/36, and the error for the left eye was + 12 D. sph. ⊂ + 1.00 D. cyl., axis 90, with visual acuity of 6/60. The right cornea was clear; the left cornea had a fairly dense central nebula. The family history was negative for the condition.

Comparison of photographs of the normal eye with photographs of the eye with cornea plana showed that the affected globe was approximately of normal size, the cornea was definitely smaller than normal, the line of corneoscleral junction had lost its sharp definition and the curvature of the cornea was the same as that of the sclera.

W. ZENTMAYER.

FILAMENTOUS KERATITIS AND KERATOCONJUNCTIVITIS SICCA. J. MALBRAN and A. ARRECHEA, Arch. de oftal de Buenos Aires **18:** 603 (Nov.) 1943.

The so-called filamentous, or filiform, keratitis is hard to classify as a distinct nosologic entity. Its etiopathologic features are obscure, many factors having been mentioned in its causation. Formerly it was thought that the filaments were only coagulated fibrin deposits in the cornea. Later a degenerative process of the corneal epithelium was said to be the cause. Still later it was stated that the keratitis was produced by diminished lacrimal secretion or dryness of the cornea. It was also said that the condition might exist in healthy corneas or might follow corneal ulceration or operation, and that it could also be produced by systemic conditions or disease.

The condition known as keratitis sicca is produced by a decrease or absence of lacrimal secretion, and "filaments" are at times noted.

The Sjögren syndrome of keratoconjunctivitis sicca, a general disease involving also the lacrimal glands and producing dryness of the cornea and conjunctiva, is not related to the disease discussed. If keratoconjunctivitis sicca is really a nosologic entity, there are cases of deficient lacrimal secretion accompanied with filamentous formations which could be classified with typical filamentous keratitis.

The following etiologic classification of lacrimal hyposecretion is accepted: congenital, traumatic or postoperative and spontaneous.

Without asserting that all the cases of filamentous keratitis in the literature are related to keratoconjunctivitis sicca, the authors express the belief that they probably are.

"Filamentous keratitis is a particular state of lacrimal hyposecretion or complete absence of tears, and it manifests itself under circumstances which are difficult to explain at present. The lacrimal hyposecretion is produced by diverse etiopathogenic mechanisms, but in all cases the condition could be classified as keratoconjunctivitis sicca."

To diagnose the condition, the Schirmer test should be used to determine the extent of the lacrimal section, and the slit lamp is necessary to visualize the corneal changes. Good results were obtained with ocular occlusion in 1 case,

and with Rucker's formula (a mixture of gelatin and Locke's solution) in another.

H. F. CARRASQUILLO.

Experimental Pathology

EFFECT OF RETINAL EXTRACTS ON GROWTH OF BLINDED MALE RATS. L. G. BROWMAN and A. A. BROWMAN, Proc. Soc. Exper. Biol. & Med. **57:** 171 (Nov.) 1944.

The evidence is consistent that total ablation of both eyes retards growth and sexual maturity in rats. It is possible that the eye exerts its influence on the pituitary gland, which, in turn, produces growth and gonadotropic substances. The interaction between the eye and the pituitary gland may be either through direct or indirect neural connections between the eye and the pituitary body or through a humoral mechanism. The present investigation is based on the hypothesis that a humoral mechanism is elaborated by the eyes of normal mammals which is necessary for normal growth and sexual maturity. Of the various retinal extracts of bovine retinas used by the authors, only the saline preparation yielded suggestive results in the direction of alleviating the retardation of weight and delayed sexual maturity characteristic of blinded male rats.

P. C. KRONFELD.

General Diseases

ASSOCIATION BETWEEN RETINOPATHIES AND ENCEPHALOPATHIES IN THE COMMON CARDIO-VASCULO-RENAL AFFECTIONS. D. J. LYLE, Am. J. Ophth. **27:** 1232 (Nov.) 1944.

This article, the author's thesis for membership in the American Ophthalmological Society, does not lend itself to abstracting. It has a number of good illustrations and two charts presenting the findings in the retina, heart, kidneys and urine in 41 cases.

W. S. REESE.

OCULAR SIGNS OF RIBOFLAVIN DEFICIENCY. W. J. W. FERGUSON, Lancet **1:** 431 (April) 1944.

Sydenstricker and his associates in 1940 described ocular signs and symptoms which responded to riboflavin therapy. The symptoms were photophobia, sensations of burning or roughness of the eyelids, visual fatigue and sometimes impairment of visual acuity in the absence of refractive errors or pathologic changes in the media. The commonest sign was "circumcorneal injection," often with invasion of the cornea by capillaries from the limbic plexus. Ferguson examined groups of patients with the slit lamp and discussed and made examinations in cases with Sydenstricker. He feels that misinterpretation has arisen largely through lack of experience in the use of the slit lamp, through imperfect understanding of the normal variations in the appearance and vascularity of the limbus and through inclusion of cases of corneal vascularization due to causes other than riboflavin deficiency. The mode of anastomosis of the anterior and posterior conjunctival vessels around a normal limbus varies. There are four typical varieties, which demonstrate that formation of capillary loops at the corneoscleral junction and on the limbus itself may be regarded as normal. The vascularization attributed to lack of riboflavin is an extension of the normal limbic vascular system to the true cornea. From the apexes of the existing limbic loops fine vessels run more or less toward the true cornea; these "streamers," in turn, anastomose with one another to form other loops, from which more streamers and, in turn, loops may be formed. The true cornea may thus become increasingly vascularized. These vessels run superficially, immediately under the epithelium, and are of such small caliber that they are usually invisible even with an ordinary binocular loupe. With the corneal microscope and slit lamp they show best when observed with light reflected from the iris, and they may readily be missed with direct corneal illumination. Abnormal corneal vascularization with very mild symptoms was found in 7.8 per cent of 422 persons. In 13 patients in whom the effect of riboflavin treatment was studied over an adequate period therapy resulted in cessation of the abnormal corneal circulation. No claim is made that riboflavin deficiency is the only cause of the corneal condition described.

J. A. M. A. (W. ZENTMAYER)

OCULAR COMPLICATIONS IN BRUCELLOSIS. RODOLFO LAJE WESHAMP, ROQUE A. MAFFRAND and MANUEL J. PEIROTTI, Arch. de oftal. de Buenos Aires **18:** 666 (Dec.) 1943.

The authors discuss this serious disease, which they consider a menace in their country. The malady is widespread, especially so in the northwestern region of Argentina, where a great number of goats, cattle and hogs appear to be contaminated.

In two years the authors have observed over 50 cases in 35 per cent of which ocular complications were present. The authors found that the optic nerve is frequently involved. Edema of the disk, probably the result of acute or chronic meningoencephalitis produced by the infection, is the commonest complication. At times true congestion of the papilla or optic neuritis occurs. Isolated retinal hemorrhages are occasionally seen. Muscular paralyses, most commonly of the lateral rectus muscles, the result of basilar meningitis, are present at times. Ocular examination revealed a normal condition in 12 cases.

The authors give in detail the history and observations in the cases they studied and summarize the cases reported in the literature.

H. F. CARRASQUILLO.

Hygiene, Sociology, Education and History

EDWARD JACKSON'S PLACE IN THE HISTORY OF REFRACTION. W. H. CRISP, Am. J. Ophth. **28:** 1 (Jan.) 1945.

Crisp gives a historical outline of refraction and enumerates the various papers and contributions of Jackson to this subject.

W. S. REESE.

Injuries

THE MANAGEMENT OF TRAUMATIC HYPHEMIA. R. O. RYCHENER, J. A. M. A. **126:** 762 (Nov. 18) 1944.

The author, in association with Ellett, has seen in the past eighteen years 9 patients with traumatic hyphemia, all in consultation weeks and months after blood staining and secondary glaucoma had occurred, and in none of them was any useful vision restored, even though the cornea cleared. The injured eye of 4 patients had to be removed because of intractable pain or unsightly appearance; in 1 of these patients sympathetic ophthalmitis developed and the sympathizing eye was lost. Two cases illustrating different phases of traumatic hyphemia are given. The following conclusions are reached:

"Traumatic hyphemia may be controlled by simple paracentesis of the cornea and the instillation of miotics.

"Surgery should be accomplished without delay whenever the intraocular pressure is increased or no clear aqueous is visible in the anterior chamber.

"It is possible that the use of miotics rather than mydriatics immediately after injury will result in less secondary hemorrhages and less necessity for surgical procedures."

W. ZENTMAYER.

SNAKE VENOM OPHTHALMIA. H. RIDLEY, Brit. J. Ophth. **28:** 568 (Nov.) 1944.

This interesting article describes spitting snakes, together with an account of the composition and action of snake venom in general, a report of a case of snake venom ophthalmia and a discussion of the therapeutic uses of venom.

A man aged 30 was cutting long grass in Africa with a native "scythe," when a concealed black-necked cobra raised its head and forcibly spat venom, some of which entered the patient's right eye. When he was seen twenty minutes after the injury, there was moderate conjunctival injection, with edema of the entire corneal epithelium. The lower two thirds of the cornea was opaque and showed punctate staining with fluorescein, as did two semicircular areas at the periphery of the cornea in the interpalpebral area. Sensation was absent from the cornea and remained so for five to seven days. On the fifth day the cornea was completely covered with edematous, loosely attached epithelium, which formed a pyramidal elevation. On the eleventh day the epithelium was removed, revealing an opacity in Bowman's membrane. On the fourteenth day the eye had completely recovered. Visual acuity was 6/6. There were no general toxic symptoms. A corneal opacity was present two months later.

W. ZENTMAYER.

Lens

THE PRODUCTION OF LENS SENSITIVITY IN RABBITS BY BRUCELLA INFECTION. E. L. BURKY, Am. J. Ophth. **27:** 1394 (Dec.) 1944.

Burky's experiments suggest that lens sensitization can be produced by infecting a damaged lens. They do not suggest that the brucella is the offending organism, although recent observations on patients with ocular disease indicate that it may occasionally be the sensitizing agent.

W. S. REESE.

EXTRACTION OF SENILE CATARACT. W. F. HUGHES and W. C. OWENS, Am. J. Ophth. **28:** 40 (Jan.) 1945.

Hughes and Owens summarize their results and draw the following conclusions:

"The gradual but radical changes in the technique of extraction of uncomplicated senile cataract during the past 19 years at the Wilmer Institute have brought about a steady improvement in final results. Statistical analysis of 2,086 extractions has shown that: (1) the amount of lens capsule and cortex remaining after an extracapsular extraction is directly related to the development of postoperative iridocyclitis, which, in turn, is the main factor in the production of secondary glaucoma; (2) loss of vitreous predisposes to postoperative simple detachment of the retina, persistent vitreous opacities, and iridocyclitis; (3) corneoscleral sutures reduce the incidence of incomplete closure of the wound, prolapse of iris, the amount of final astigmatism, and, with two sutures, anterior-chamber hemorrhages; (4) preservation of the round pupil reduces the likelihood of vitreous loss; (5) diabetes of long standing or requiring 30 units of insulin or more per day predisposes to the development of severe anterior-chamber hemorrhages, but there is no correlation between the height of the bloodsugar and postoperative complications; (6) syphilis, either treated or untreated, and systemic hypertension have no significant influence on the occurrence of postoperative complications."

W. S. REESE.

Lids

RECONSTRUCTION OF THE LOWER LID BY HUGHES' METHOD. J. FOSTER, Brit. J. Ophth. **28:** 515 (Oct.) 1944.

Foster reports 2 cases of basal cell carcinoma of the lower lid, unsuitable for irradiation, in which the procedure described by Hughes was employed. In the first case the final step of the operation could not be carried out, as the patient met with accidental death. In the second case the general cosmetic and functional results were satisfactory.

The article is illustrated. W. ZENTMAYER.

CONGENITAL ECTROPION ASSOCIATED WITH BILATERAL PTOSIS: CASE REPORT. S. GORDON, Brit. J. Ophth. **28:** 520 (Oct.) 1944.

Gordon reports a case of congenital ectropion of all four lids, with associated ptosis of the upper lids. The facial bones were normal. A satisfactory correction of the defects was obtained by inserting into each upper lid a thin Thiersch graft cut from the arm and into the lower lids a Wolfe graft of postauricular skin. Four months later facial slings attaching the upper lids to the frontalis muscle overcame the ptosis.

The article is illustrated. W. ZENTMAYER.

PTOSIS. V. D. SATHAYE, Indian J. Ophth. **4:** 54 (July) 1943.

In a case of bilateral ptosis it is necessary to know whether the levator muscle is completely, or only partially, paralyzed and whether there is only paresis of Müller's muscle.

In a case of monocular ptosis it is essential to determine whether the condition is real or apparent. Paralysis of the superior rectus muscle of one eye with a spasm of the inferior oblique muscle of the affected eye may give the appearance of ptosis. The differentiation can be made by holding up both upper lids and asking the patient to close the eyes firmly. Normally the eyes will roll up in so doing.

W. ZENTMAYER.

Neurology

TUBEROUS SCLEROSIS. M. D. SACHS and D. A. SHASKAN, Am. J. Roentgenol. **52:** 35 (July) 1944.

According to Sachs and Shaskan, tuberous sclerosis is a rare hereditary disease of ectodermal origin. Tuberous sclerosis, Recklinghausen's neurofibromatosis and trigeminal nevus with angioma of the brain are distinct neurocutaneous syndromes. Of the three, tuberous sclerosis presents the most clearcut clinical, roentgenologic and pathologic picture. It is most frequently associated with mental retardation and epileptic seizures. The authors describe a case of tuberous sclerosis in a white soldier aged 32. The cardinal findings in this case, with a history of epileptic seizures, were adenoma sebaceum; fibromatous nodules on the forehead, scalp and back; a pigmented, hairy nevus of the lumbar area; vitiligo of the left thigh and the left side of the back; phacoma of the retina, and "cotton ball" calcifications of the brain, right greater trochanter and fifth lumbar vertebra. The authors think that delay in the diagnosis of tuberous sclerosis is probably due to the physician's unfamiliarity with the syndrome because of its comparative rarity.

J. A. M. A. (W. ZENTMAYER)

NEUROSYPHILIS AND THE OCULIST. A. C. ESPOSITO, M. Bull. Vet. Admin. **21:** 51 (July) 1944.

Esposito describes the routine for examination of the eyes followed at Chillicothe, Ohio. The confrontation test for the field of vision is found satisfactory, and especially suited to the more deteriorated type of patients.

In the series of 218 patients with neurosyphilis, 14 had on preliminary examination some impairment, such as optic nerve atrophy, field defects or failing vision, which contraindicated tryparsamide therapy; of the remaining 204 patients who were placed under treatment with tryparsamide, symptoms of drug toxicity involving the optic nerve developed in 26. The author reaches the following conclusions:

All patients with neurosyphilis should be referred to the oculist before their treatment is begun. Each such patient should be returned for examination of the visual fields, central vision and fundi after each of the first ten injections of tryparsamide during the first and each subsequent course of treatment. Administration of tryparsamide should be permanently discontinued at the first sign of a toxic reaction involving the optic nerve. Malaria therapy, with later treatment with trivalent arsenical and bismuth preparations, should be instituted for the patients showing reactions. W. ZENTMAYER.

Ocular Muscles

REPAIR FOLLOWING TUCKING OPERATIONS ON THE EXTRAOCULAR MUSCLES. K. S. CHOUKÉ, Am. J. Ophth. **28:** 50 (Jan.) 1945.

Chouké gives the following summary:

"After a tucking operation the two adjacent sides of the loop of muscle join together by means of fibrous connective tissue. The side of the muscle nearest the eyeball quite often, but not always, becomes attached to the sclera by fibrous connective tissue. The process of repair of

extraocular muscles in the dog is essentially similar to that of the skeletal muscles elsewhere in the body. The time required for the completion of repair of extraocular muscles is slightly longer than that for general skeletal muscles of the same animal. The continuity of the muscle is preserved after the tucking operation, as evidenced by response to electrical stimulation."

W. S. REESE.

DEFINITION OF ANOMALOUS RETINAL CORRESPONDENCE. K. C. SWAN, Am. J. Ophth. **28:** 58 (Jan.) 1945.

Swan summarizes his discussion as follows:

"The prevalent definition of abnormal retinal correspondence as an anomaly in which the fovea of the fixating eye and a peripheral retinal area in the squinting eye become functionally corresponding points seems erroneous. Studies of the field of binocular vision reveal that the peripheral retinal area in question is almost invariably suppressed.

"Unless there is a high degree of amblyopia the macular region of the squinting eye is only partially suppressed; consequently, demonstration that the foveal or macular regions of the two eyes are not corresponding points provides a practical method of diagnosing anomalous retinal correspondence in the great majority of patients. Afterimages, stereoscopic devices, or a filter projection system may be utilized to stimulate the macular regions and to determine their relative visual directions.

"Anomalous retinal correspondence is not necessarily fixed at a constant angle of anomaly, but is frequently variable and tends to adapt itself to the deviation of the eyes. Experience with several hundred cases indicates that instead of completely disrupting abnormal retinal correspondence, muscle surgery alone usually results in a gradual change in the angle of anomaly to correspond with the new deviation.

"Another characteristic of anomalous retinal correspondence is that it becomes unstable with disuse; that is, disruption of binocular vision. Prolonged monocular occlusion is an important adjunct in treatment of the anomaly.

"In accordance with these findings, anomalous retinal correspondence is defined as an anomaly of binocular vision in which areas in the two retinas normally having a common visual direction—for example, the foveas—acquire an unstable and often variable visual direction in relation to each other but usually in accordance with the squinting position. The anomaly is always associated with some degree of suppression of the squinting eye, the point of fixation almost invariably being viewed monocularly."

W. S. REESE.

Orbit, Eyeball and Accessory Sinuses

AN OPERATION FOR SHRUNKEN SOCKET. J. KRAUS, Brit. J. Ophth. **28:** 224 (April) 1944.

The operation consists essentially in a dissection of the conjunctiva from the floor of the orbit, the implanting of a skin graft and the use of a cavity dilator which produces a circular force from within outward. The space between the margins of the lids remains unaltered, and the maximum pressure is exerted well within the socket, with diminishing force along the retractor blade, toward the lid margins. The steps of the operation are well illustrated in the article.

W. ZENTMAYER.

MUCOCELE OF MAXILLARY ANTRUM. G. E. DODDS, Brit. J. Ophth. 28:510 (Oct.) 1944.

The condition was observed in a Nigerian native. A swelling was situated just above the lower margin of the orbit and could be palpated for a certain distance into the orbit. It gave the typical sensation of a fluid-containing cyst and was but slightly movable from side to side. The globe was displaced upward. Definite proof that the diagnosis was mucocele of the antrum has not so far been obtained in this case.

The article is illustrated. W. ZENTMAYER.

Retina and Optic Nerve

OBSTRUCTION OF THE CENTRAL RETINAL VEIN. B. A. KLIEN, Am. J. Ophth. **27:** 1339 (Dec.) 1944.

Klien attempts to correlate clinical and histopathologic data in this study. She presents 17 cases and concludes that primary phlebosclerosis plays a greater role in venous occlusion than has heretofore been supposed. The site of the most extensive proliferative endophlebitis is frequently the anterior lamina cribrosa. Anticoagulant and antispasmodic therapy gives more promise for the younger patients. W. S. REESE.

OPHTHALMOSCOPIC CLASSIFICATION OF HYPERTENSIVE DISEASES. G. E. CLAY and M. BAIRD, Am. J. Ophth. **27:** 1396 (Dec.) 1944.

Clay and Baird discuss hypertension and outline a classification. They conclude that the greatest need is that of a commission to formulate a proper nomenclature and classification of hypertensive disease. W. S. REESE.

CLINICAL STUDIES IN ANGIOSPASM. I. GIVNER, Am. J. Ophth. **27:** 1408 (Dec.) 1944.

Givner presents 3 cases of angiospasm, each representative of a type. He discusses these cases from the standpoint of prognosis and diagnosis and suggests that future investigations in

such cases include pupillographic studies to gain information as to the part the hypothalamus plays.

W. S. REESE.

Tumors

BILATERAL METASTATIC CARCINOMA OF THE CHOROID WITH X-RAY THERAPY IN ONE EYE. F. C. CORDES, Am. J. Ophth. **27:** 1355 (Dec.) 1944.

Cordes gives the following summary:

"1. A case is reported of a woman, aged 31 years, who had bilateral metastasis to the choroid secondary to a scirrhous carcinoma of the breast.

"2. One eye was enucleated and the diagnosis confirmed by microscopic examination.

"3. With the appearance of a similar growth in the second eye x-ray irradiation was employed. This was followed by disappearance of the tumor and retention of 20/20 vision in the eye. Fourteen months later there was a recurrence. The eye was again irradiated, with regression of the tumor.

"4. Employing x-ray therapy to the eye made it possible for the patient to retain 20/20 vision up to the time of death (23 months).

"5. While the ultimate prognosis is hopeless, the possibility of retaining useful vision by means of palliative irradiation should receive consideration in cases of metastatic carcinoma of the choroid."

W. S. REESE.

DIAGNOSIS OF ORBITAL TUMORS. W. L. BENEDICT, J. A. M. A. **126:** 880 (Dec. 2) 1944.

This is the address of the guest of honor of the Section on Ophthalmology of the American Medical Association, read at the Ninety-Fourth Annual Session.

The article does not lend itself to abstraction and should be read in the original. Benedict supplies the following summary and conclusions:

"The probability of tumor in any case of exophthalmos is so great that only in cases of goiter is there serious doubt of the presence of an expanding lesion. The temptation to explore the orbit is irresistible for some surgeons and an exploration is planned. This is not a surgical procedure but a diagnostic one unless the surgeon is prepared to remove the tumor and do the necessary repair. Exploration by trocar is useless and should never be done. Such a procedure is of no help in diagnosis, and in case of malignant tumor or vascular aneurysm it is positively dangerous. Puncture for digital exploration only should never be practiced. One cannot explore the orbit with the finger from any one place along the rim and be sure that nothing has been missed. Exploration of the orbit for diagnosis should always be done through an incision large enough and so placed that, should a tumor be encountered or any other pathologic condition be found that would require surgical removal, the operation can be completed at the time. If one is not sure of the presence of a tumor, it is in most instances safe to employ roentgen therapy and await developments."

W. ZENTMAYER.

THE GENETICS OF RETINOBLASTOMA. A. D. GRIFFITH and A. SORSBY, Brit. J. Ophth. **28:** 279, 1944.

At the Royal Eye Hospital, London, 59 children with retinoblastoma were seen between 1894 and 1943. Only one familial group has now been observed over three generations, with 6 cases of the disease. The condition was bilateral in 15.1 per cent of cases.

Analysis of the literature shows that the mode of inheritance is irregularly dominant. The incidence of bilateral involvement appears to be higher for the genetic type of retinoblastoma than for the sporadic type. It is possible that hereditary retinoblastoma is a distinct histologic entity, differing from the sporadic types.

W. ZENTMAYER.

UNILATERAL AND BILATERAL RETINOBLASTOMA: A POSSIBLE HISTOLOGICAL DIFFERENCE. J. W. CUMMINGS and A. SORSBY, Brit. J. Ophth. **28:** 533 (Nov.) 1944.

In an attempt to answer the question whether genetic retinoblastoma is histologically different from the sporadic variety, the authors studied 21 cases. Two cases were excluded as instances of unusual tumor formation. The remaining 19 cases consisted of 8 instances of unilateral retinoblastoma, 8 instances of bilateral retinoblastoma and 3 cases of hereditary retinoblastomas. From the study it is suggested that unilateral retinoblastoma originates in the outer nuclear layer, while the bilateral tumors are derived from both nuclear layers or, possibly less frequently, from the inner nuclear layer. In the 3 cases of hereditary retinoblastoma the tumors were bilateral and did not appear to differ from the sporadic bilateral retinoblastoma.

The article is illustrated.

W. ZENTMAYER.

Uvea

GONORRHOEAL IRIDO-CYCLITIS TREATED BY PENICILLIN, WITH REPORT OF A CASE. A. J. ELLIOT, Canad. M. A. J. **51:** 257, 1944.

A man aged 28 was treated for acute gonorrheal urethritis and secondary gonorrheal arthritis with sulfadiazine. On the eleventh day of treatment administration of the drug was discontinued because of the presence of casts in the urine. During the time of treatment iridocyclitis developed in the right eye. The iris was bound down by posterior synechias. After unsuccessful efforts to free the synechias with sub-

conjunctival injections of a solution containing epinephrine hydrochloride (1:4,000), cocaine hydrochloride and atropine sulfate, treatment with injection of 500 units of penicillin through the cornea was given for five days, together with intravenous injections of penicillin, in a dose of 15,000 units every three hours. Local application of atropine was continued; at the end of this time the pupil was widely dilated and vision had improved from perception of hand movements only to 20/15. The arthritis did not respond to the penicillin therapy.

W. ZENTMAYER.

Vision

AMBLYOPIA IN CASES OF READING FAILURE. T. H. EAMES, Am. J. Ophth. **27:** 1374 (Dec.) 1944.

Eames gives the following summary:

"The records of 100 cases of reading failure were compared with those of an equal number of children who were known to be passing in their school studies. A considerably greater incidence of amblyopia was found among the poor readers, and they exhibited a greater average amount of amblyopia in the left eye only. The average amount of amblyopia in the right eye only and in both eyes was the same in each group."

W. S. REESE.

THE EFFECT OF THE DURATION OF STIMULUS ON THRESHOLD MEASUREMENTS IN THE DARK ADAPTED EYE. S. YUDKIN, Brit. J. Ophth. **28:** 611 (Dec.) 1944.

Yudkin describes the instrument used and the method of carrying out the test and supplies the following summary and conclusions:

Five groups of 60 to 115 men were tested on each of three occasions. The thresholds for the dark-adapted rods of all the men were measured, using a test light exposed in flashes of 0.2 second's duration. In addition, the thresholds for the men in each group were tested with a light exposed in flashes of one of the following durations: 0.02, 0.04, 0.1, 0.5 and 1 second.

The following results were obtained:

The mean threshold was lower for the longer durations up to 0.5 second, but the lowering of the threshold was not proportional to the increased duration of exposure. The range of thresholds for all the groups was the same whatever the exposure. The variability of individual thresholds from test to test was least with the 0.2 second exposure.

The results given here are probably applicable to all measurements of threshold made with similar instruments.

W. ZENTMAYER.

Vitreous

CYSTIC FORMATIONS IN THE VITREOUS BODY: A CLINICAL CASE. JOSÉ SAENZ CANALES, An. Soc. mex. de oftal. y oto-rino-laring. **17:** 123 (July-Aug.) 1942.

Canales refers to this anomaly as an ophthalmologic curiosity since it is rarely seen by the oculist, as it does not alter the normal condition of the eye and the patient does not seek medical advice unless some intercurrent condition is present.

The following classification of cysts of the vitreous is made: cysts located in the anterior part of the vitreous, near the crystalline lens; cysts located in the posterior part of the vitreous, in the vicinity of the optic disk, and cysts free in the vitreous body.

Of the first type the following subtypes are considered: (1) cysts produced by anterior remains of the fetal hyaloid vascular system, a lesion which may or may not be associated with opacities in the crystalline lens; cysts produced by remains of the anterior portion of the canal of Cloquet, and cysts of ciliary origin, which may be congenital or acquired.

Of the second type the following subtypes are defined: cysts formed by posterior remains of the fetal hyaloid vascular system; cysts representing the posterior remains of the canal of Cloquet; cysts formed by mesodermal remains of the fetal cleft, and cysts of uveal origin, which may be congenital or acquired.

Of the third type, two subtypes, congenital and acquired, are described.

Detailed descriptions of the appearance of all these cysts are given, and numerous citations from the literature are made. The differential diagnosis is well discussed.

The author reports a clinical case. A patient aged 32 complained of poor vision for distance, which was worse in the right eye. Visual acuity in the left eye was 7/10 and could be improved to 8/10 with the pinhole disk; in the right eye it was 4/10 and could not be improved. Both eyes showed opacities in the vitreous, as well as well defined, disseminated pigmentary changes in the retinas; a cystic formation was observed in the region of the papilla in the right eye. The author diagnosed the lesion as a cyst of the vitreous and classified it as a cyst formed by the posterior remains of the fetal hyaloid vascular system. The pigmentary changes he believed to be hereditary, probably syphilitic. General physical examination revealed nothing significant.

H. F. CARRASQUILLO.

Society Transactions

EDITED BY DR. W. L. BENEDICT

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

WARREN S. REESE, M.D., *Chairman*

GEORGE F. J. KELLY, M.D., *Clerk*

April 19, 1945

Conservation of Lid Margins During Blepharoplasty. DR. CHARLES A. RANKIN.

The author presented the history and treatment of a white boy aged 17 years.* The middle half of one upper lid had been cut away by flying metal in an explosion in a chemical laboratory. Particles of lid margin were reunited by dovetailing. Further and complete reconstruction of the lid with use of skin and mucous membrane grafts was carried out. The final result showed a well conserved, smooth, even lid margin, with no notching or overcorrection. The cilia were well placed.

DISCUSSION

DR. EDMUND B. SPAETH: Much good plastic work on the eyes has been spoiled by an attempt "to gild the lily." It is as important to know when not to operate further as to know when to operate and what to do.

Esser, Wiener, Wheeler and others have written much on the conservation of lid margins in ophthalmic plastic work. Elschnig and Snellen both spoke many years ago of dovetailing separate flaps. As far as I know, the case presented by Dr. Rankin is the first instance of separate attention to the margin of the lid and to that portion of the lid above the margin. It is a procedure which can be utilized basically in many traumatic lacerations of the lid, I am sure.

DR. JAMES S. SHIPMAN: I think there are no operations performed about the eye by the general hospital intern that cause more harm and lead to more plastic repair in the future than those on wounds of the eyelid. Fortunately, this patient was seen at the start by some one who realized the seriousness of the condition. I think we ophthalmologists who are associated with general hospitals can do much to prevent the necessity of future plastic repair by instructing the general intern to refrain from sewing up the eyelid when the laceration goes through the margin of the lid.

Angioid Streaks Observed over a Period of Thirty-Six Years: Report of a Case. DR. WILLIAM ZENTMAYER.

In the case of angioid streaks first observed by Dr. Zentmayer in 1908 and seen at varying intervals since, the last time in May 1944, the right eye showed masses of dense pigment of irregular shapes. In some portions of the fundus there was complete atrophy of the choroid. The gray zone which was formerly observed about the papilla had disappeared, and there was no longer any trace of angioid streaks. The papilla was somewhat waxy in appearance.

In the left eye, the general appearance of the fundus was similar to that of the right eye; only the areas of complete destruction of the choroid were more extensive, and there was denser massing of pigment. Beneath the superior temporal retinal artery there was a vertical lesion, about 3 disk diameters in length, which had the appearance of the lesions associated with circinate retinitis. The papilla was waxy in appearance.

Vision was 1/60 in each eye. The patient had suffered a stroke affecting his speech. The systolic blood pressure was 210 mm. of mercury.

The condition of angioid streaks is probably due to degeneration of Bruch's membrane, with which tearing is associated, and the hemorrhages result from similar changes in the walls of the blood vessels. All other changes in the fundus are a part of the syndrome. The association with pseudoxanthoma elasticum occurs with such frequency that it may be assumed that the two conditions have a common pathologic basis.

Factors in the Examination of Astigmatism. DR. I. S. TASSMAN.

Certain difficulties are sometimes encountered in the accurate determination of the kind and amount of astigmatism and also in the exact determination of the axis of the correcting cylinder. Probably for this reason, a great deal of stress is laid on procedures and tests for making these determinations by subjective examination. The examination and correction of ametropia cannot be reduced simply to a single mathematical or mechanical procedure. Important factors in the examination of the patient include a proper and thorough analysis and evaluation of the subjective symptoms. Such symptoms include headache, dizziness, double vision and blurring. Whenever these symptoms are complained of, it should first be determined whether they are

the result of, or are associated with, ametropia, particularly astigmatism.

Hyperopic astigmatism causes more discomfort than myopic astigmatism, except when the latter is of low degree. The amount of accommodative effort employed is an important factor in the production of symptoms in cases of hyperopic astigmatism. It is also an important factor in cases of convergent strabismus. In the latter, the deviating eye invariably presents a greater amount of hyperopic astigmatism, usually at an oblique axis, while in the fixing eye there may be little, if any, astigmatism.

In young children with fairly high hyperopic astigmatism in one eye and little, if any, astigmatism in the other eye, amblyopia may occur very early, whether or not a deviation is present. In most cases of astigmatism in young children of early school age, symptoms and complaints may be absent. In older children and in young and middle-aged adults, subjective symptoms resulting from the presence of hyperopic astigmatism are more common. In very old patients who use the eyes only moderately for close work, a considerable degree of astigmatism may be present without troublesome symptoms. The occupation of the patient, the accommodation and the type of astigmatism bear an important relationship to the presence of symptoms. Young people who do close work constantly and who have hyperopic astigmatism which requires the use of a great deal of accommodation will usually complain of headache and ocular fatigue.

A cycloplegic should be employed in refraction with all young patients. In all cases of astigmatism, whether a cycloplegic is employed or not, retinoscopy should provide the basic determination of the refractive error and the axis of astigmatism. The best method for this purpose is what is known as "cylinder retinoscopy," at 1 meter. However, whether spherical or cylindric retinoscopy is used, the preliminary determination by either method should not be neglected. In cases of irregular astigmatism with corneal opacities, scissors motions, immature changes in the lens and other alterations in the media, difficulties may be encountered in obtaining an accurate result with retinoscopic tests. In these cases retinoscopic examination at a closer distance is recommended to obtain the best possible result.

In cases in which a cycloplegic is used the subjective test should follow the objective test, and in cases of average astigmatism the results should correspond. In young children the result of a careful retinoscopic examination is more dependable than the result of a subjective test, and it is arrived at in a much shorter time. Postcycloplegic examination should follow the cycloplegic test. This should provide the final result. Here, the cross cylinder can be employed in some cases as an auxiliary in checking the axis of the cylinder and the strength of the combination. The astigmatic dial can also be employed as an auxiliary or as a preliminary test with some selected patients, but it does not eliminate the need for careful retinoscopic tests in routine practice.

DISCUSSION

DR. ALFRED COWAN: I should like to emphasize what Dr. Tassman said about the procedure known as cylinder retinoscopy. This is probably the most accurate objective test known for persons for whom one has to depend entirely on objective tests. It is the only way to determine objectively the amount of astigmatism and the axis of the cylinder.

I agree with Dr. Tassman here, but I do not agree that the importance of the subjective examination should not be overemphasized. I do not think one can overemphasize its importance. After all, in cases in which one can make a subjective test, the subjective test is all-important. No objective test can be conclusive, no matter how well it is done or by whom. With the subjective test one can probably come nearest to the exact refraction.

DR. I. S. TASSMAN: I think that today much emphasis is placed on subjective tests while other important factors and the objective examination are more or less neglected. As I stated in the paper, the subjective test provides the final result, but I am afraid that there has been a tendency during the past few years, in the examination of many patients, to underestimate and neglect the objective tests. Dr. Cowan stated that "with the subjective test one can probably come nearest to the exact refraction." This depends a great deal on the intelligence and power of discrimination of the patient, which are frequently found to be lacking. I also mentioned such factors as the accommodation, the age and occupation of the patient and the nature of the symptoms as important in properly recognizing and evaluating the nature of the condition present.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

THOMAS H. JOHNSON, M.D., *Chairman*

WENDELL L. HUGHES, M.D., *Secretary*

March 19, 1945

Toxoplasmosis: Report of Two Cases. DR. RAYMOND L. PFEIFFER.

Toxoplasmosis should be considered in the etiologic study of chorioretinal disease. The possibility of toxoplasmosis constitutes another indication for roentgenography in cases of suspected retinoblastoma.

DISCUSSION

DR. FERDINAND L. KOCH: It is gratifying to learn from Dr. Pfeiffer's excellent report that

other examiners are finding the diagnosis of toxoplasmosis warranted in certain instances. Drs. Wolf, Cowen, Paige and I, after our original report on the ocular findings in this protozoal entity, almost doubted for a time whether we had seen any of these lesions. We knew very well, of course, that we had, but few others appeared to find them.

Since we did not wish to be too enthusiastic, publication of our report was delayed for more than a year in order to confirm and recheck the individual diagnoses by serologic tests on those patients who had not come to autopsy. One should, however, be conservative in making a diagnosis of toxoplasmosis merely on the basis of the serologic results.

DR. RALPH I. LLOYD: In 1890, Lindsay Johnson described a group of cases of a condition which he named extrapapillary coloboma, to distinguish it from the type connected with defective closure of the optic fissure. The features noted were a sharp, clearcut margin with normal surrounding tissue, pigment anterior to the vessels and irregular pigmented lines against the bare sclera. Since then, Treacher Collins, Ida Mann and Arnold Sorsby have studied cases both clinically and microscopically. Collins and Sorsby describe the condition as a defective development of the choroid, while Ida Mann states that it is the result of intrauterine inflammation. Ida Mann divides the disease into three types: that with pigment border and pigment against the sclera; that with ectasia of the sclera, and that with vessels of the ciliary or the choroidal region emerging from a defect and ramifying in the retina. She gives a different date of origin for each type: the second month of gestation, for the last type; the fourth to the fifth month, for the second type, and the sixth month, for the first type. Other arguments for the congenital origin of the defect is that it runs in families and that the mixing of retinal vessels with the other types is not duplicated in disease. Clinical experience has taught the necessity of differentiating these defects from healed tuberculosis of the choroid and from a type of hereditary macular degeneration. Now that toxoplasmosis has been studied and defects of the fundus shown to be part of the disease which are similar to some previously considered as congenital, an effort should be made to review past experience and determine whether this form known as extrapapillary coloboma should be subdivided. That lesions of this type could be the result of choroidal disease in infancy does not seem possible to me. On the other hand, the claim that this disease can exist in the embryo and damage the developing eye cannot be dismissed without careful consideration. It does seem that these defects must be prenatal in origin because of associated errors of development found in some cases, like apical dystrophy of the phalanges, malformations of facial bones, retinal folds, choroidal defects about the optic disk and pigment clumps scattered throughout the fundus.

DR. ARNOLD KNAPP: Apparently, in all cases in children, areas of calcification in the brain were demonstrable in the roentgenograms of the skull. I should like to ask Dr. Pfeiffer whether these calcifications are also found in defective or premature infants when this lesion of the retina is not present.

I think the most interesting part of the presentation is the suggestion that toxoplasmosis occurs in adults and that the diagnosis can be made from the ophthalmoscopic picture. I feel that one should be hesitant in making this diagnosis, because, as Dr. Pfeiffer says, the roentgenograms of the skull in adults are negative and the diagnosis can be confirmed only by a serologic test, which, as far as I know, is still not definitely accepted.

DR. RAYMOND L. PFEIFFER: In answer to Dr. Knapp's questions: Few premature babies have been studied roentgenographically in my laboratory, so that I cannot speak from personal experience. I should think, however, that one ought not to expect to find these deposits of calcium in the brain of a child simply because it is premature. So many children with toxoplasmosis are born prematurely, and, certainly, the finding of these deposits, with their irregular and strange distribution, which does not follow any particular order and may be found anywhere throughout the brain substance, is strong evidence of toxoplasmosis. In fact, I think one can make the statement, as I already have, that the coexistence of these deposits and the ocular findings described is diagnostic of toxoplasmosis. As I explained, the serologic test has not as yet been fully evaluated, so that the diagnosis of toxoplasmosis in an adult is still open to question.

Clinical Differentiation of Emboli in the Retinal Arteries and Endarteritis. DR. ARTHUR J. BEDELL.

This article will be published in full in a future issue of the ARCHIVES.

Paralysis of Elevation with Real Blepharoptosis and Pseudoblepharoptosis. DR. DANIEL B. KIRBY.

This article will be published in full with discussion in a later issue of the ARCHIVES.

The Surgical Limbus. DR. HENRY MINSKY.

The difficulties in choosing properly the site of the keratome section in operations for glaucoma are due to the inherent obscuration of the angle of the anterior chamber by the scleral overhang which forms the anatomic limbus of the cornea. Since this overhang varies in different persons, no numerical designation is always adequate.

Most surgeons enter the anterior chamber too far forward, thereby failing to deliver the root of the iris into the wound. When the iridectomy is performed, a bridge of the iris tissue is left behind, as Reese has pointed out.

The surgical limbus, as opposed to the anatomic one, can be easily demonstrated by focal illumination of the corneal margin contralateral to the site of incision. If a focal beam of light is made to impinge on the limbus at 6 o'clock, the upper limbus glows by internal reflection in the cornea. The outside margin of the glow on the sclera represents the projection of the hidden clear cornea. If the point of the keratome is placed at the periphery of the surgical limbus and entered into the eyeball in the plane of the iris, it will reach the angle of the anterior chamber.

Anatomic evidence was presented in slides to show the relationship of the limbic glow to the angle of the anterior chamber. A microscopic slide showed that the tract of the keratome wound, when made in this way, was placed just in front of the base of the iris.

Two photographs of an intercalary rupture of the cornea with prolapse of the iris were shown: the first, as usually taken; the second, demonstrating the glow of the surgical limbus. The prolapse was precisely at the outer margin of the surgical limbus, proving the validity of the experimental work.

The practical importance of this method is found in the security the surgeon feels when he makes his incision in cataract extraction, in the Lagrange operation and in basal iridectomy.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Ophthalmological Society of Mexico and College of Medicine of National University of Mexico.—On joint invitation from the Ophthalmological Society of Mexico and the College of Medicine of the National University of Mexico, Dr. Daniel B. Kirby, of New York, gave a series of lectures and surgical clinics in México, D. F. The lectures were given at the Cardiology Institute, and the surgical clinics were held at the Hospital de la Luz, April 16 to 27 inclusive. Forty-five Mexican ophthalmologists attended the course, at the completion of which the dean of the College of Medicine and the rector of the university made Dr. Kirby an honorary professor of ophthalmology.

Sociedade de Oftalmologia de Minas Geraes.—The Sociedade de Oftalmologia de Minas Geraes on April 7, at the São Geraldo Hospital, elected the following officers for the year 1945-1946: president, Dr. Geraldo Queiroga; vice president, Dr. Amelio Bonfioli; secretary, Dr. Guilherme Fonseca; treasurer, Dr. Helio Faria.

Sociedade de Oftalmologia de São Paulo.—The Sociedade de Oftalmologia de São Paulo elected the following officers for 1945-1946: president, Dr. Silvio de Almeida Toledo; vice president, Dr. Penido Burnier Filho; general secretary, Dr. Plinio Toledo Piza; secretary, Dr. Moacir Cunha; treasurer, Dr. Aureliano Fonseca; filing, Dr. Orlando Aprigliano.

New York Academy of Medicine, Section of Ophthalmology.—The new officers of the section are:

Chairman: Dr. Rudolf Aebli, 30 East Fortieth Street, New York; secretary: Dr. Truman L. Boyes, 654 Madison Ave., New York.

The meetings will held at 8:30 p. m., on the third Monday of every month from October to May, inclusive.

Book Reviews

Modern Ophthalmic Lenses and Optical Glass. By Theodore E. Obrig. Third edition. Price $4.50. Pp. 323, with 180 illustrations, charts and tables. Philadelphia: The Chilton Company, 1944.

This excellent treatise was fully reviewed in the ARCHIVES (**14:** 315 [Aug.] 1935) when it first appeared, in the same year. The third edition is fully revised and includes improvements in optical glass and in spectacle lenses and a description of contact lenses, telescopic spectacles and newer types of bifocals. These are all subjects of practical importance to the ophthalmologist. The book is an up-to-date treatise and contains information which is important and often difficult to acquire. For this the author has placed the reader in his debt, and many will find this manual instructive and useful.

CORRECTION

In the article by Dr. Charles A. Bahn entitled "Ophthalmic Requirements of the Military Services: Changes from Jan. 1, 1944 to Jan. 1, 1945," which appeared in the March issue (ARCH. OPHTH. **33:** 245, 1945), the table on page 245 should have appeared under that section of the article entitled "C. Air Corps: Flying."

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

Faculty of Ophthalmologists

President: Brig. Sir Stewart Duke-Elder, 63 Harley St., London, W. 1, England.
Secretary: Mr. Frank W. Law, 45 Lincoln's Inn Fields, London, W. C. 2., England.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. John Foster, 45 Park Sq., Leeds.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of South Africa

President: Dr. A. W. Sichel, National Mutual Bldg., Church Square, Cape Town.
Secretary: Dr. J. K. de Kock, Groote Kerk Bldg., 32 Parliament St., Cape Town.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Prof. Moacyr E. Alvaro, Consolação 1151, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

SCOTTISH OPHTHALMOLOGICAL CLUB

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Arturo Etchemendigaray, Villa Constitución, Santa Fé.
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

SOCIEDADE DE OFTALMOLOGIA E OTORRINOLARINGOLOGIA DE RIO GRANDE DO SUL

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
In compliance with the request of the Office of Defense Transportation and in the interest of the national war effort a meeting will not be held in 1945.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Watson Gailey, 1000 N. Main St., Bloomington, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Theodore L. Terry, 140 Marlborough St., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. James H. Mathews, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Roekford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912-9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val. H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N. St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. George P. Meyer, 410 Haddon Ave., Camden.
Secretary: Dr. John P. Brennan, 429 Cooper St., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Pennsylvania Academy of Ophthalmology and Otolaryngology

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.

Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.

Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.

Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.

Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.

Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.

Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.

Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.

Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.

Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn 16.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Samuel J. Meyer, 58 E. Washington St., Chicago 2.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.

Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. M. Paul Motto, Rose Bldg., Cleveland.

Secretary: Dr. H. H. Wygand, Guardian Bldg., Cleveland.

Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. Erwin W. Troutman, 21 E. State St., Columbus, Ohio.

Secretary-Treasurer: Dr. T. Rees Williams, 380 E. Town St., Columbus 15, Ohio.

Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.

Time: 6:30 p. m., third Tuesday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.

Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.

Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.

Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.

Secretary: Dr. Cecil W. Lepard, 1025 David Whitney Bldg., Detroit 26.

Place: Club rooms of Wayne County Medical Society.

Time: First Wednesday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.

Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.

Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.

Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.

Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.

Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.

Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Dennis Smith, 623 Security Bldg., Long Beach 2, Calif.

Secretary-Treasurer: Dr. Robert Null, 710 Security Bldg., Long Beach 2, Calif.

Place: Seaside Hospital. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Secretary-Treasurer. Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach 2, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.

Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Thomas H. Johnson, 30 W. 59th St., New York.
Secretary: Dr. Wendell L. Hughes, 131 Fulton Ave., Hempstead, N. Y.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Maurice L. Wieselthier, 117 E. 30th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York 28.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Secretary: Dr. Robert J. Billings, 509 Liberty Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Isaac B. High, 326 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Eye, Ear, Nose and Throat Society

President: Dr. Luther C. Brawner, Professional Bldg., Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. Vincent Jones, 634 N. Grand Blvd., St. Louis.
Secretary: Dr. T. E. Sanders, 508 N. Grand Blvd., St. Louis 3.
Place: Oscar Johnson Institute. Time: Fourth Friday of each month from October to April, inclusive, except December, at 8:00 p. m.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.

Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.

Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.

Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.

Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.

Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.

Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.

Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.

Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.

Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.

Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. L. C. Ravin, 316 Michigan St., Toledo 2, Ohio.

Secretary: Dr. W. W. Randolph, 1838 Parkwood Ave., Toledo, Ohio.

Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.

Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.

Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Harold M. Downey, 1740 M St. N. W., Washington, D. C.

Secretary-Treasurer: Dr. Richard W. Wilkinson, 1408 L St. N. W., Washington, D. C.

Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.

Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.

Place: Office of chairman. Time: Last Tuesday of each month from October to May.